Lumleian Lectures
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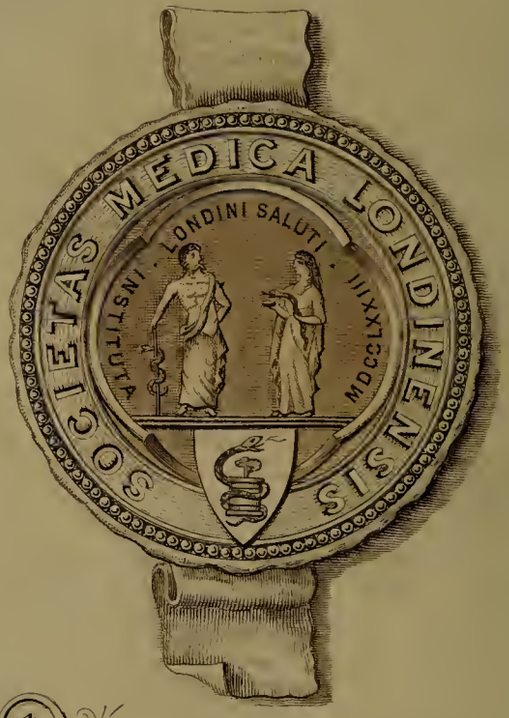
Some Physiological Points in the Pathology and Clinical History of Pneumonia

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THE LUMLEIAN LECTURES

ON

# Some Moot Points in the Pathology and Clinical History of Pneumonia

Delivered before the Royal College of Physicians of London
on May 30th and June 4th and 6th, 1912

BY

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# LECTURE I.

*Delivered on May 30.*

MR. PRESIDENT, FELLOWS AND GENTLEMEN,—An invitation to deliver the Lumleian lectures before this College is at once an honour and an embarrassment—an honour to be allowed to follow in the footsteps of my illustrious predecessors in this lectureship, but an embarrassment when one recalls the high standards of the past. I shall not detain you with a superfluous profession of my unworthiness of so important an office, but before addressing myself to the subject of my lectures it is my pleasing duty to express my grateful thanks to you, Sir, and to the Censors of the College, for entrusting me with this honourable and onerous task.

Pneumonia is a well-worn topic, but it possesses a perennial fascination. I can only plead that I have fallen under its spell. I am fully conscious of a sense of temerity in attempting, before such an audience, to deal with so well-known and so large a subject. But although our knowledge of the disease has received considerable addition in recent years, many gaps still remain to be filled in.

## DEFINITION.

The classification of pneumonia is beset with difficulties, whether the basis adopted be anatomical or etiological. The anatomical conception of the malady as a lobar affection has been of service, but it has this disadvantage that lobar pneumonia may be counterfeited by confluent lobular areas of consolidation—pseudo-lobar pneumonia, as it has been called. An etiological basis is, no doubt, the most scientific and is the necessary complement of the former. But while bacteriology has already shed much light on the pathology of pneumonia,

and may be expected to shed still more in the future, there are many points in the etiology of the disease which cannot yet be explained in terms of bacteriology.

Clinical medicine seeks to combine as far as possible the anatomical and the etiological. Pneumonia in its typical form may be described from the clinical standpoint as an acute febrile disease beginning in most cases abruptly, less often insidiously, associated with massive consolidation of the lung, running a fairly definite course, and terminating within ten days by crisis or lysis.

The overwhelming majority of cases answering to this description are due to a specific microbe, but difficulties arise from the fact that the same organism may be the cause of pneumonias which run a far less definite course, and also from the fact that lobar pneumonia may be the result of more than one cause. Consequently for clinical purposes our definition must be somewhat wider, and must include cases of acute febrile disease accompanied by massive consolidation of the lung. It is in this wider sense that I propose to use the term.

## Etiology.

The view that pneumonia is a specific fever, and is more than a mere local disease of the lung, is not new. But it was not until the end of last century that bacteriology supplied an actual demonstration of the truth of this doctrine. Klebs was the first to discover microbes in pneumonia, and subsequently Eberth and Koch found cocci in the lungs and blood of pneumonic patients. But the independent researches of A. Fränkel, Talamon and Weichselbaum first demonstrated the existence of a specific organism, a capsulated diplococcus, the *Diplococcus pneumoniæ*, *Streptococcus lanceolatus*, or pneumococcus. This diplococcus was isolated in pure culture from pneumonic lung, the culture when inoculated into animals giving rise to a general infection, with diplococci in the blood and in the different organs. Friedländer had previously described another microbe which he had

frequently found in pneumonia, a short, capsulated, rod-shaped organism, since known as Friedländer's bacillus, or the *Bacillus pneumoniæ*. The staining and cultural characters of Friedländer's bacillus and the pneumococcus are very different, the former microbe also being much less pathogenic to animals. It was subsequently shown that the pneumococcus is identical with the coccus of sputum septicæmia, and also that it is a normal denizen of the throat in a considerable proportion of healthy persons.

Fränkel asserted the doctrine of the unity of pneumonia —that is to say, that all lobar pneumonia is due to the pneumococcus. This view has been widely adopted, in spite of the fact that Weichselbaum, as the result of an extensive series of observations, had come to a different conclusion, which he formulated in 1886. According to Weichselbaum [1], the virus of pneumonia is not a single one. Lobar pneumonia may be caused by various kinds of microbes, among which are *Diplococcus pneumoniæ*, *B. pneumoniæ* (Friedländer), *Streptococcus pneumoniæ*, identical with *S. pyogenes*, and *Staphylococcus pyogenes*. The pneumococcus, or *Diplococcus pneumoniæ*, is by far the commonest cause of acute primary pneumonia. But this micro-organism, like the other microbes alluded to, may also be found in secondary inflammations of the lung and in acute broncho-pneumonia.

### Results of Experimental Inoculations.

From the first, all workers in the field of experimental inoculation with cultures of the diplococcus have agreed that in laboratory animals, such as the mouse and rabbit, the result is a rapidly fatal septicæmia in which diplococci are found in the blood and organs generally. When considerable doses of the diplococcus are injected, and when virulent cultures are employed, the animal dies in three days or less from septicæmia without any local lesion beyond swelling of the spleen.

With smaller doses and with less virulent cultures, in-

flammatory lesions are found at the seat of inoculation, but the animal succumbs to a septicæmia. When cultures of low virulence are inoculated into the pleura or peritoneum, fibrinous exudations are produced, from which the animal dies in several days, or it may recover. In this case no septicæmic symptoms arise.

In none of the above conditions are definite pulmonary changes produced. If, however, cultures be injected into the trachea, or be inhaled, the lungs show hyperæmia and partial consolidation, but not true fibrinous pneumonia. But in resistant animals like the rat, large doses of cultures injected subcutaneously are said to give rise to considerable areas of consolidation resembling croupous pneumonia [2].

Wadsworth [3] found that in rabbits partially immunized by injections of pneumococcal cultures subsequent intratracheal injections of virulent diplococci did not give rise to general infection; but if the animal were not too highly immunized caused pulmonary lesions comparable to those of lobar pneumonia in man. Similar lesions have been produced in the sheep and dog, which are very resistant to the pneumococcus, by direct injection of pneumococcal culture into the lung. But the conditions here are so entirely different from those met with in pneumonia in the human subject that the experiments are of little value. Quite recently Lamar and Meltzer [4] have succeeded in producing fibrinous lobar pneumonia in dogs by intrabronchial injections of bouillon culture of pneumococci. The anatomical features varied according to the stage of the disease and corresponded to the stages found in man.

Man is evidently endowed with great powers of resistance to the pneumococcus, as shown by the high percentage of recovery in pneumonia. Further, in cases comparable to pneumococcal septicæmia of animals, recovery is not uncommon in the human subject. It appears, therefore, that in the more acute pneumococcal infections, in which the cultures are very virulent, and in

the more sensitive animals, the pneumococcus causes a septicæmia from which the animal rapidly dies without any marked local changes in the organs. In more resistant animals the septicæmic condition is less marked or absent, and fibrinous exudation occurs in the lungs and serous membranes as in man.

But it has been shown that most of the localized complications of pneumonia are due to the diplococcus, such as meningitis, peritonitis, pericarditis, bronchitis, endocarditis, otitis, &c. Moreover, in many instances a primary meningitis, pericarditis, peritonitis has been proved to be pneumococcal when the lungs had escaped entirely. The same is true of inflammations apparently primary of other parts—rhinitis, tonsillitis, conjunctivitis, orchitis, prostatitis, cystitis, enteritis, thyroiditis.

Mention may here be made of an extensive research, conducted by Királyfi [5], of Budapest, in Professor Bordet's laboratory in Brussels, on pneumococcal infection in guinea-pigs. Királyfi finds that, contrary to the usually accepted statement, this animal is very susceptible to infection. Of the twenty-five guinea-pigs inoculated subcutaneously with pure cultures a few recovered, one was killed six days afterwards, the rest died twenty-four hours to seven days after infection. The results of his experiments confirm the conclusion of clinical observers that the heart is specially liable to suffer in pneumococcal infection. In cases of rapidly fatal septicæmia without any gross lesions of any organ, microscopical examination of the heart shows definite changes in the myocardium or in its interstitial tissue. The first change observed is a dilatation of the capillaries and small arteries. At a later stage capillary hæmorrhages occur, and somewhat later œdema of the myocardium with dilatation of the lymphatics associated with proliferation of their endothelial cells. Numerous lymphocytes are found in the œdematous areas, a fact which stamps the œdema as inflammatory, although no diplococci are found in the muscular walls. Œdema is most marked

near the arterial ostia, where fibrous tissue is most abundant. In no case was endocarditis found. In many cases the heart was flabby and dilated. This dilatation could not be ascribed to inflammatory or degenerative myocardial changes, as dilatation was present in cases showing nothing more than circumscribed œdema and dilatation of lymphatics and small blood-vessels. It was only in cases that survived for several days that pronounced degenerations of the myocardium could be recognized. In most cases pericarditis was present, the exudation consisting of fibrinous threads containing lymphocytes and scanty diplococci in their meshes. Islets of small-celled infiltration between the muscular fibres were very common. In some instances the myocardium had undergone softening, and in one case extensive coagulative necrosis resulted. The suprarenal capsules were in almost every case found to be the seat of hyperæmia and hæmorrhage. Changes in the lungs were rarely observed, and when present they consisted of microscopical collections of small cells round the capillaries. Subcutaneous injection of pneumococcal cultures was rapidly followed by an extensive inflammatory œdema at the seat of inoculation.

## Sources of Diplococci.

It has been shown that pneumococci can be found in the throats of a large proportion of healthy persons, and the virulence of the organisms has been proved by inoculation of susceptible animals. The virulence of the diplococci thus obtained can be increased by successive passages through suitable animals like the mouse.

By analogy we may conclude that successive passages through human subjects must largely add to the virulence of any given strain of pneumococcus. This may help to explain the pernicious character of the disease in some epidemics of pneumonia. According to Park and Williams [6], a lower percentage of strains of diplococci virulent for rabbits was obtained from the throats of normal per-

sons than from cases of pneumonia. Netter found that the diplococci of healthy saliva are most virulent during those times when the mortality from pneumonia is highest.

The strains of diplococci obtained from different sources vary considerably in virulence, as many observers have found. In artificial cultivations the microbe soon loses its pathogenic properties. Virulence can only be preserved by frequent passage through susceptible animals, the mouse in particular. But in dried sputum the diplococcus maintains its pathogenic properties for a considerable time. Kolle and Hetsch [7] state that when the dried sputum is exposed to diffuse sunlight, the organisms may maintain their activity for fifty-five days. If dried sputum or blood be kept in a dry place and protected from light, the diplococci may remain virulent for months or years. The resistance of the microbe under these conditions is attributed to the protective influence of its albuminous coating. The pneumococcus is very resistant to cold, but is very sensitive to moist heat, being killed by a temperature of 52° C. in ten minutes. It is also easily destroyed by the ordinary disinfectants. But the resistance varies much with different strains.

Luetscher [8] finds that diplococci obtained from the pharynx in cases of pneumonia have the same virulence as those obtained from the sputum, whereas strains obtained from the pharynx after resolution has taken place and expectoration has ceased have a relatively low grade of virulence. He ascribes this loss of virulence to an unfavourable action of the saliva.

The main sources of supply of the diplococcus seem to be the cavity of the mouth and throat of healthy people and the sputum of pneumonic patients. Considering the highly resistant character of the microbe in dried sputum and the wide diffusion of the latter, the opportunities of infection must be very considerable.

Whether pneumonia is excited by the entrance into the body of dried sputum containing diplococci from

without, or whether it is to be attributed to auto infection with germs constantly present in the throat-is still uncertain. It seems somewhat difficult to believe that the continued presence of diplococci in the throat would not lead to the establishment of a certain degree of immunity against infection with the particular strain, whereas the entrance of a different and perhaps more virulent strain of pneumococcus from external sources might, under certain conditions, be able to cause infection.

## Mode of Infection of Lung: Aerogenic Theory.

If the sources of the diplococci are not in doubt the same cannot be said of the method by which the lung is affected.

The view most widely held is that the microbe is inhaled into the lung. This view presents some difficulties. From the wide distribution of the germs, whether in the throats of living people or in the form of atmospheric dust, the microbe must frequently be inhaled with the air, and yet pneumonia is a more or less exceptional occurrence. Some other conditions favouring the development of the diplococcus, some disposition, has therefore been assumed.

That bacterial organisms can pass into the lungs through the air passages is proved by an experiment of Nenninger [9], in which guinea-pigs were exposed to a spray of a culture of *Micrococcus prodigiosus* for ten minutes. The animals were killed immediately afterwards by puncture of the medulla, careful precautions against regurgitation of oral secretions into the air passages being taken by clamping the trachea. Cultivations were made from the periphery of the lung, a part which contains only alveoli and smaller bronchi. A plentiful growth of the micrococcus was obtained, showing that the germs had been inhaled into the lungs. Weichselbaum, Babes and others have found that the

lungs of healthy animals contain no microbes, or at the most were few. Paul believes that under ordinary circumstances diplococci which enter with the air are destroyed in virtue of a bactericidal action of the lungs, failure or impairment of this action leading to infection This view is adopted by Weichselbaum. The seasonal incidence of pneumonia in the late winter and early spring months when alterations of temperature are very rapid, commonly attributed to diminished power of resistance, may be explained on this hypothesis by a corresponding failure of bactericidal action.

Some light has been thrown on the part played by chilling of the surface in the production of pneumonia by experiments on guinea-pigs and rabbits. Artificial cooling of these animals, immediately before or after intratracheal injections of cultures or pneumonic sputum, was followed by infection, whereas negative results were obtained with animals that were not so exposed to cold.

Weichselbaum explains these results as being due to rapid circulatory disturbances modifying the bactericidal action, and he invokes a similar explanation for cases of traumatic pneumonia. The pneumonia which occasionally attacks persons rescued from drowning was ascribed by Fränkel to mechanical damage to the epithelial lining of the alveoli ; but Weichselbaum considers that sudden cooling may be the cause. Löwy and Richter found that animals previously injected with tissue juices that excited leucocytosis survived the injection of two or three times the fatal dose of a pneumococcal culture.

The special frequency of pneumonia in the months with the greatest variability of temperature may also be connected with a widespread prevalence of catarrh at these times, favouring an increase of the virulence of diplococci present in the throat.

But the lobar distribution of pneumonia remains to be accounted for. In pneumonoconiosis, which is undoubtedly the result of the entrance of finely divided particles through the bronchi, the pulmonary lesions are

not lobar, but discrete, nodular, peribronchial. The same is true of pulmonary tuberculosis, which is generally attributed to inhalation of infective dust into the bronchioles. We should rather expect on the aerogenic theory that virulent diplococci in their passage through the bronchi to the lung would excite some bronchitis. But it is well known that in many cases of pneumonia there are no signs or symptoms of bronchitis whatever. The experimental production of lobar pneumonia in certain animals by intratracheal or intrapulmonary injection of pneumococcal cultures cannot be regarded as affording conclusive evidence in favour of the aerogenic theory in man, for the conditions are not fairly comparable.

Another view that has been put forward is that the germs entering the bronchi pass into the bronchial glands and thence invade the lung. The constant changes in the bronchial gland in pneumonia have been cited in support of this view, but the glandular affection may with more probability be regarded as secondary to the pulmonary.

### Hæmatogenous Theory.

Others, following Jürgensen, believe that the microbe when inhaled passes into the blood and causes a septicæmia, becoming subsequently localized in the lung. It has been also suggested that the diplococci obtain direct entrance to the blood-stream from the throat. But in neither of the last two cases is any indication given of the route by which the pneumococcus enters the blood. In favour of the septicæmic origin of pneumonia, it has been urged that in many cases symptoms of a general constitutional character precede the development of local symptoms or signs of disease of the respiratory organs by some days. Indeed, instances are known in which physical signs of pneumonia do not appear until the time of the crisis. The current explanation of this fact assumes that the morbid process

in the lung was deeply seated, and did not approach the surface until the disease was nearly at an end. This explanation may be valid for some cases, but it cannot account for all—for example, for pneumonia of the apex of the upper lobe, the thickness of this part of the lung being so slight as to preclude the notion that consolidation could long elude physical examination.

In a joint publication entitled "Pneumococcémies," Lemierre, Abrami, and Joltrain [10] contribute two very important cases bearing on this question. In both instances the patients were admitted suffering from severe constitutional symptoms without any signs or symptoms of pulmonary disease. Both patients were admitted with the diagnosis of typhoid fever, one on the eighth the other on the fourth day of the illness. The blood was examined on the day of admission in each case, and gave a negative result to the Widal test, but in both a pure culture of diplococci was obtained in twenty-four hours. On the tenth day in both cases the patient complained of pleuritic pain, and signs of pneumonia appeared. Slow recovery ensued in each instance. The authors regard these cases as strong evidence of the hæmatogenous origin of pneumonia. In the first case diplococci were found in the blood two days, in the second case six days, before the appearance of symptoms or signs of pneumonia. They remark that some Italian and German observers have found diplococci almost constantly in the blood of pneumonic patients. Prochaska [11] found them in almost every case he examined.

Widal found them only in one out of four cases, Memmi in 80 cases obtained a positive result in 25 per cent. Wiens [12] believes that the presence of pneumococci in the blood is practically constant, the success of the cultivation depending on the nature of the culture medium. In a total of 33 cases examined by him, the result was positive in 26. In 30 of these cases, using blood agar as medium, 13 were positive. In 15 cases with peptona medium, 13 were positive. In 6 cases

cultivated in a special peptone dextrose fluid medium, all 6 were positive. In some instances, especially with mild cases, it may be necessary to incubate the blood for 48 hours in the peptone dextrose fluid.

Wiens thinks the conclusion is warranted that bacteriæmia in croupous pneumonia is constantly found when a suitable culture medium is employed. Consequently he holds that the discovery of bacteriæmia possesses only a limited prognostic significance. A large number of pneumococci in the blood generally warrants a grave prognosis, but a small number may be found in grave and fatal cases. In such circumstances nervous symptoms of toxæmic origin are generally present. Pneumococci do not disappear from the blood with the cessation of fever, but may persist for twenty-four hours or more. In view of the constant presence of pneumococci in the blood, the description of cases of pneumonia with bacteriæmia as pneumococcal sepsis is unnecessary. This term should be reserved for cases of pneumococcal infection, where septic symptoms predominate, and pulmonary manifestations are absent, or are merely a part of the general infection.

Roedelius [13] arrives at somewhat different conclusions, preferring solid media for the detection of germs in the blood—agar and glucose agar. In 335 clinical blood tests he found the pneumococcus in 64 = 19·1 per cent. In 69 *post-mortem* blood tests he obtained a positive result in 51 = 83·9 per cent. Of the 64 cases in which pneumococci were found in the blood during life, 29 recovered, 35 died. In general, cases with bacteriæmia were severe. The number of germs in 2·0 c.c. of blood varied greatly, there being a clear relation between the severity of the disease and the number of the microbes. In cases examined frequently the pneumococci were found to appear and disappear repeatedly. The chief conclusion of this paper is that entrance of the germs into the blood-stream is by no means invariable.

Lemierre, Abrami, and Joltrain (*loc. cit.*) also point out that lesions limited to the pulmonary alveoli, as is usual in pneumonia, can hardly be explained otherwise than by a hæmatogenous origin. The marked tendency of pneumococcal infection in man to provoke changes in the lung offers no more difficulty than is presented by the determination of the typhoid process to the intestines, or of tuberculosis to the lungs, both supplying illustrations of the tissue proclivities of different microbes, as pointed out by Follet and Sacquépée [14].

A case by Boulloche in which pneumococcal arthritis and myositis were followed by lobar pneumonia five days later, and similar experiences of Segré and of Desguins, in which the lung was presumably infected through the blood, are also cited in support of the hæmatogenous origin of pneumonia. The occasional occurrence of lobar pneumonia in the new-born infants of women suffering from pneumonia, where the diplococci can only have gained access to the fœtus through the blood, is another case in point.

Guided by the analogy of tuberculosis—where, according to Calmette's view the tubercle bacilli reach the lung through the intestine—Calmette, Vansteenberghe and Grysez [15] introduced virulent cultures of diplococci through an œsophageal tube into the stomach of guinea-pigs. The animals, when killed at the end of twenty-four hours, showed congestion of the lungs, and scrapings of the lung tissue contained abundant diplococci. In rabbits a similar procedure gave like results, though the pulmonary engorgement was less intense. If finely divided carbon particles were added to the cultures, the lungs in twenty-four hours showed diffused anthracotic changes. But in no case were lobar pneumonic lesions produced. Control animals treated in the same way recovered in a few days. The authors believe that in man pneumonia is due to hæmatogenous infection, the diplococci being swallowed and passing through the thoracic duct into the blood-stream.

If we compare the different views that have been expressed it seems from the early date at which diplococci may be found in the blood, and from the clinical evidence that pneumonia so often appears for some days under the guise of a general infection without local manifestations, that a septicæmic origin supplies the best explanation. But the exact route by which infection of the blood takes place has yet to be demonstrated.

## Immunity.

Among the many remarkable characteristics of pneumonia none is more striking than the sudden termination, whether in death or recovery. All observers are agreed that death is commonly due to circulatory failure, though whether this is the result of cardiac or vasomotor paralysis is still a matter of dispute. A knowledge of the steps by which recovery takes place involves a comprehension of the process of immunity.

Kolle and Hetsch, in their text-book, point out that after recovery from pneumococcal infection man acquires a certain degree of immunity against the pneumococcus. But this immunity is neither absolute nor persistent, for patients who recover from severe pneumonia may again contract pneumococcal infection more than once in some form or other. Still, in most cases some protection is conferred. In animals, also, prolonged treatment with pneumococcal cultures gives immunity. Some workers seem to have succeeded in immunizing rabbits with dead or attenuated cultures or with filtrates of cultures, but the best method of immunization consists in the intravenous injection of living virulent culture, beginning with very small quantities and cautiously increasing the dose. As to the explanation of this immunity opinion is divided. Experiment shows that the blood serum of immunized animals and the serum of human convalescents from pneumonia contain substances possessed of immunizing action. The formation of these substances was stated by Wassermann to

take place almost exclusively in the bone marrow. But Dr. Bulloch informs me that later experience has shown that the elaboration of antibodies is not the monopoly of any tissue, but is a widely distributed property, largely developed in the subcutaneous tissues. By injecting small quantities of human convalescent serum into rabbits and mice protection is conferred against simultaneous injection of such quantities of diplococci as prove rapidly fatal to control animals, and cure may even be effected in animals that already show clear signs of infection. The protective action of the serum is not dependent on antitoxic substances, for the poisons of the pneumococcus not being soluble are not discharged from the microbe, but are intimately bound up with the bacterial cell, *i.e.*, they are endotoxins. Moreover, the formation of antitoxic substances in the immunized human or animal body in response to the presence of endotoxins is not abundant. It must be concluded, therefore, that the action of the serum is antibacterial. And, as shown by Neufeld and Rimpau, specific bacteriotropic substances in pneumococcal serum possess a certain importance. The above extract from Kolle and Hetsch gives a concise statement of the present position as regards immunity. Luetscher (*loc. cit.*) concludes that the crisis of pneumonia is not the result of any change in the virulence of the pneumococci, for as long as these microbes are expectorated they retain practically their original virulence.

Attempts have been made to gain some insight into the causation of immunity by a study of the blood serum of pneumonic patients before and after the crisis. Seligmann and Klopstock [16] examined the pre-critical and post-critical serum by the method of complement fixation. In the pre-critical serum they expected to find the presence of antigen, in the post-critical serum of antibodies. As the result of their observations, conducted with necessary control experiments, in no case were they able to recognize any fixation of complement, and even in a fatal case

of pneumonia, where presumably there must have been an increase of antigen, they failed to find any. Further, making use as a test of Römer's polyvalent pneumococcal serum, whose richness in specific antibodies could be determined by experiments with pneumococcal extracts, they were unable to detect any antigen either in pre-critical or post-critical serum. Extracts of the spleen and of red hepatized lung in a fatal case of pneumonia showed the presence of antigen when tested with Römer's serum. Extracts of pneumococcal cultures used as artificial antigen reacted with Römer's serum but not with pneumonic serum, whether before or after the crisis. Experiments made to test the protective power of pneumonic serum in white mice against inoculation with pneumonic sputum gave a negative result. Seligmann and Klopstock conclude that a closer insight into the nature of the pneumonic crisis has not been obtained by these experiments, and that their results furnish no experimental proof of the interaction of antigen and antibodies in pneumonia.

Neufeld and Haendel [17], in an eleborate research on the origin of the crisis in pneumonia and on the immunizing action of pneumococcal serum, come to a very different conclusion. In opposition to Seligmann and Klopstock, they believe that the crisis not only depends on the formation of antibodies, but that these antibodies can be recognized experimentally with certainty, and may even be estimated quantitatively. The antibodies found in the blood of convalescents from pneumonia behave in exactly the same way as those artificially produced in animals. The practical application of pneumococcal serum for therapeutic purposes depends on the preparation of a sufficiently powerful serum and on the rapid introduction of the same into the body in sufficient quantities. For this purpose they recommend as indispensable intravenous injection of large quantities of serum, which, according to recent experience, is free from danger. The authors' experiments with the serum

of convalescents from pneumonia were conducted on white mice in the same way as in the case of protective animal serum. They were unable to test the serum of a large number of patients recovering from pneumonia, but in every case examined they were able to detect the existence of antibodies, so that their presence may be regarded as invariable. In one case the result at first seemed to be negative, but this was explained later by the discovery that the pneumonia in question was caused by an atypical strain of pneumococcus. When the patient's serum was tested with this strain it proved to contain abundant antibodies. The serum was always tested as to its protective action against the same standard strain of pneumococcus. This strain, which manifested a constant degree of virulence, was almost invariably used for the preparation of their protective serums. Comparative experiments were made with a fixed quantity, 0·2 c.c., of pneumonic serum, normal human serum, and serum of immunized horses and asses. The result showed that pneumonic serum possessed a marked protective power, much greater than normal human serum, though less than that of the immunized horse or ass. In one case the post-critical serum showed a strongly protective action in mice and rabbits, whereas the pre-critical serum from the same case had no definite effect. The serum of horses and asses immunized by intravenous injections of liquid virulent cultures possesses not only a protective but also a curative action. It is suggested that the negative results of Seligmann and Klopstock's protective experiments—in which pneumonic sputum and convalescent serum were mixed and injected together into mice—may be explained by the unsuitable nature of the method.

Seligmann and Klopstock, with the method of complement fixation, failed to find antigen in the pre-critical serum of pneumonia or complement-fixing antibodies in the post-critical serum, though in pneumonic lung and sputum antigen was found which fixed complement with

Römer's pneumococcal serum. But, as Neufeld and Haendel point out, these observations do not disprove the participation of bacteriotropic substances in the causation of the crisis, but they rather point to bacteriotropins as the only antibodies that are concerned. As pneumococci are usually destroyed mainly in cells, and are not set free and dissolved in the serum, it is easy to understand why extracts of organs contain antigen, while the serum does not. But this last conclusion does not follow directly from Seligmann and Klopstock's experiments, for the development of complement fixation often requires the presence of considerable quantities of antigen. Moreover, as bacteriotropins do not fix complement, there is no reason why complement-fixing substances should be present in the serum of convalescents.

That the crisis of pneumonia depends on the development of antibodies seems to admit of no doubt.

## Crisis.

G. and F. Klemperer, under the influence of Behring's discovery, conceived that in pneumonia the poisonous action must depend on a toxin analogous to the diphtherial toxin, and that the removal of the toxin at the crisis must be due to its neutralization by an antitoxin. Numerous experiments have proved that in every case of pneumonia the diplococci pass into the blood, and therefore into other organs, and the general condition of the patient shows that they develop marked toxic action. Whereas it has not been certainly proved that definite toxic effects can be produced by killed cultures or by filtrates of diplococci, experiments *in vitro* show that living cocci, in virtue of their vital activity, exercise a rapidly destructive action on red corpuscles and leucocytes. In all probability a similar action is exerted on other cells of the body.

If we now suppose that, in consequence of a copious development of bacteriotropins, the cocci growing in the

blood and organs are devoured by phagocytic cells, the result is that the further growth of the cocci and the consequent intoxication are suddenly arrested, although the complete destruction of germs in the interior of cells must take somewhat longer. An explanation is needed of the fact that the antibodies developed in pneumonia, as a rule, bring about a rapid critical method of cure in contrast with the slow recovery in other infectious diseases in which also antibodies presumably play the chief part.

In Neufeld and Haendel's researches it was repeatedly found that the most powerful antiserums, when given in less than a certain dose, fail to confer any protection. In white mice 0·2 c.c. serum (*i.e.*, $\frac{1}{100}$th of body weight of a mouse) protects against 0·1 c.c. of culture—*i.e.*, against nearly one million times the fatal dose. With proportionally smaller doses both of serum and of culture, the results are far less satisfactory, and a point is soon reached when the reduced amount of serum fails entirely to protect against minimal doses of cultures, or shows a very uncertain action.

In protective experiments the quantitative relations are very striking. The law of multiples does not hold good, only very large doses of serum protect from large doses of culture, small doses of serum have no corresponding effect on weaker infections, and with a further diminution of the serum all effect ceases. In man attempts at cure can only be expected to give good results with large doses of serum, and the addition of antibodies in less than a certain quantity will not, as in diphtheria, give less decided results, but probably will have no action at all. It is not the case here, as in diphtheria, that a definite quantity of antibodies neutralizes approximately an equal amount of virus. But as soon as the antiserum injected is diluted beyond a certain limit by its distribution throughout the body it ceases to have any action whatever, at any rate at first, until the development of antibodies takes place in the infected organisms.

It is necessary, therefore, that pneumococcal serum

should be administered exclusively by intravenous injection, and in as large doses as possible. The amount of the dose can only be determined by experiment. In mice the full action of the protective serum is only obtained in a dilution of not more than 1 in 100—viz., 0·2 c.c. in a mouse weighing about 20 grammes. But the same proportion must not without more ado be assumed for man, who is much more resistant to pneumococcal infection than laboratory animals. It is probable that the pneumococcal antibodies can exert their influence in a much higher dilution in man than in the mouse.

The peculiar quantitative relations observed in the action of the various serums throw some light on the nature of the virus. We may suppose that in the course of the disease antibodies are formed, but at first are almost without effect, until a certain concentration is reached. But then with a further accumulation of antibodies an action is exerted, not merely in proportion to the increasing concentration, but much more rapidly. The result is that the cocci circulating in the blood and germinating in the various organs are rendered harmless in a short time by phagocytosis.

I have tried to give a rather full account of Neufeld and Haendel's views, for they seem to be very important, and no brief statement could do them justice. The fact that they have succeeded in conferring a high degree of protection against the pneumococcus in the mouse, perhaps the most sensitive of all animals to this infection, is a very remarkable achievement. These experiments raise hopes that, in spite of the disappointing experience of serum treatment in the past, improvements in this method may yet give good results. But in the event of further therapeutic experiments in this direction it will be well to bear in mind these authors' recommendations as to the dose and the method of administrations of the serum. We must look to the bacteriologists to provide us with a suitable serum.

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## LECTURE II.

MR. PRESIDENT, FELLOWS, AND GENTLEMEN, — It would obviously be impossible on this occasion to discuss more than a few of the many clinical problems presented by pneumonia. In the present lecture, therefore, I have selected certain topics for consideration without attempting to deal with the disease as a whole. This statement, I hope, will explain the somewhat disconnected character of my observations.

### RESPIRATION.

The respiration in pneumonia presents many interesting features which can be better studied in children than in adults. In some adults the breathing is comparatively little affected, whereas in children this is never the case. In the latter increased rate of respiration is a constant symptom, and is more conspicuous than in adults.

The absence of all subjective sensation of dyspnœa in a child breathing at the rate of 60 to the minute is a striking fact which has been noted by many physicians. The same thing may be observed in uncomplicated pneumonia in adults with marked acceleration of respiration. In such cases the breathing is superficial and almost entirely abdominal. The inverse rhythm of respiration, in which the pause occurs after inspiration instead of expiration, expiration being sometimes accompanied by a grunting sound, is often met with. In children suffering from pneumonia, and less commonly in adults, respiration is not infrequently accompanied by active rhythmical expansion of the alæ nasi.

The foregoing facts have been subjected to a careful consideration by Dr. G. A. Sutherland [1] in a lecture on lobar pneumonia in children. Speaking of the action of the alæ nasi he says :—

"We all recognize a slight inspiratory dilatation of the nares in early childhood, and a marked increase of this dilatation when any obstruction of the respiratory passages is present. This is characteristically seen in catarrhal pneumonia. In all writings on lobar pneumonia one finds mentioned an exaggerated movement of the alæ nasi, and when this is described it is stated to be an inspiratory dilatation.

"My own observations have led me to believe that there is no such inspiratory dilatation of the nares in uncomplicated pneumonia, because there is no pulmonary obstruction. Nevertheless, there is in pneumonia an exaggerated movement of the alæ nasi, but it consists of an expiratory dilatation. It is not the exaggerated physiological movement, but an exactly reverse condition. It occurs during, or at the end of, expiration, and it occurs only in association with the inverted type of respiration. The method of its production is probably as follows. In the inverted type of breathing the expiration is forcible and air is driven out with a certain explosive force, so that the air rushing through the nose distends the lax alæ nasi."

Since reading these remarks of Dr. Sutherland my attention has been more specially directed to this action of the alæ nasi. I can confirm his statement that in some cases of pneumonia in children, and in adults also, the expansion of the alæ nasi is not inspiratory. As Dr. Sutherland points out, it is often difficult, in children breathing rapidly, to time accurately the exact position of the respiratory act at which the alæ nasi dilate. But by utilizing a method recommended by him I have lately found that the timing of the movements is greatly facilitated. Dr. Sutherland's method consists in holding the mouthpiece of a binaural stethoscope in front of the patient's nose, when the loud expiratory sound can be sharply distinguished from the much weaker sound of inspiration.

In a recent case of pneumonia in an adult, a man,

aged 30, breathing with normal rhythm at the rate of 40, auscultation by Dr. Sutherland's method in front of the patient's nose clearly demonstrated that the elevation of the alæ nasi, which was very vigorous, occurred at the end of expiration, or rather during the pause between expiration and inspiration. This was confirmed in a general way by placing the hand on the abdomen. But if the timing had depended solely on the application of the hand to the abdomen, the action of the alæ nasi would certainly have been regarded as expiratory, as it occurred alternately with the descent of the diaphragm.

It is possible that if I had employed this method in previous cases in which the expansion of the nostrils was regarded as expiratory, it might have been shown to take place during the pause. Dr. Sutherland's statement that the expiratory elevation of the alæ nasi only occurs with the inverted rhythm of breathing in children has been mentioned. This does not seem to be the case in adults, and I have seen one or two children who exhibited that symptom with a normal respiratory rhythm. The explanation that this action is due to the explosive force of expiration is further invalidated by the fact that the nostrils expand during the latter part of expiration when the pressure is lowest. I regret that I am unable to offer any better explanation myself.

An interesting observation was made in the case of a child, aged 11 months, suffering from pneumonia of the right upper lobe; pulse 140, respirations 60. The respiratory rhythm was inverted, but the breathing was superficial, almost entirely abdominal, and unaccompanied by any distress. The alæ nasi acted vigorously during the latter part of expiration. Three days later this child was much worse, very pale, and somewhat livid. Pulse 180, respirations 66. In addition to the signs of consolidation of the right upper lobe, there were abundant crepitations over the whole right back and at the left base. The breathing was now of normal rhythm, but markedly laboured, the intercostals and accessory

muscles of inspiration being in full play, and the lower intercostal spaces were drawn in with inspiration. The elevation of the alæ nasi was still vigorous, but now took place during the early part of inspiration. In this case at first, while the breathing was superficial and easy, the alæ nasi acted during expiration, whereas as soon as pulmonary obstruction appeared, the action was reversed, and occurred during inspiration, thus bearing out Dr. Sutherland's observations.

No satisfactory explanation of the inverse rhythm of respiration has yet been given. Dr. Eustace Smith has suggested that this rhythm and the grunting expiratory sound are the result of pleuritic pain, the child holding its breath and letting it go with a grunt. But, as Dr. Sutherland shows, this form of respiration may be present without any pain. Dr. Sutherland quotes the following remarks by Hughlings Jackson on a case of "latent pneumonia" :—

"I suggest that the central lesion is the cause of the non-pulmonary symptoms of pneumonia, the high temperature, rapid respiration, and infrequent pulse (infrequent, I mean, only in relation to the respiration rate). I do not think the local pulmonary inflammation would produce such symptoms in such relation."

Adopting Hughlings Jackson's suggestion, he refers the respiratory and cardiac symptoms of uncomplicated early pneumonia to toxæmic disturbances of the respiratory and cardiac centres in the medulla. The effects of these are likened to the results of experimental section of the vagus and stimulation of its central end, in which case the respiration becomes rapid and superficial, and the heart is slowed. Although the pulse-rate in pneumonia is always raised, yet in relation to the respiration it is relatively slower. This view would explain the early development of tachypnœa with a very limited lesion in the lung, and also the want of relation between the area of lung involved and the frequency of respiration. Hughlings Jackson held that automatic breathing is of

medullary origin, and in males certainly is chiefly abdominal, whereas voluntary breathing is of cortical origin, and is chiefly upper costal. This would explain, as Dr. Sutherland points out, why it is that in uncomplicated pneumonia the disturbance of the respiratory centre in the medulla produces exaggerated abdominal breathing without any consciousness of dyspnœa, and why thoracic breathing is not apparently altered in any way.

## Sputum.

The naked-eye appearances of the sputum of pneumonia are described in every text-book, and require no notice here. But in most books the microscopical characters receive slight attention, and the descriptions given are rather vague.

Sir William Osler [2], who gives one of the fullest accounts, says :—

"Microscopically the sputum consists of leucocytes, mucus corpuscles, red corpuscles in all stages of degeneration, and bronchial and alveolar epithelium. Hæmatoidin crystals are occasionally met with. Of micro-organisms, the pneumococcus is usually present, and sometimes Friedländer's bacillus and the influenza bacillus. Very interesting constituents are small cell moulds of the alveoli and the fibrinous casts of the bronchioles; the latter may be plainly visible to the naked eye, and sometimes may form good-sized dendritic casts. Chemically the expectoration is particularly rich in calcium chloride."

Dr. Pye-Smith and Dr. Beddard [3] write as follows :—

"On microscopical examination the sputum consists of mucus from the bronchial tubes mixed with the contents of the alveoli and infundibula. Besides structureless mucus, there are abundant red cells and leucocytes, together with a few epithelial cells and fibrinous plugs from the smallest bronchioles. When treated by appropriate stains, the pneumococcus is revealed."

A recent study of the microscopic characters of the

sputum by De Jong [4] has added considerably to our knowledge. For the details of the technique adopted by him, reference must be made to his monograph. The use of Unna's polychromatic blue stain has enabled him to differentiate certain constituents of the sputum with great sharpness. On examining films of the rusty sputum of an early case of pneumonia (second to third day) stained with this dye two fundamental points arrest attention—the peculiar appearance of the basis of the sputum, and the scarcity of cellular structures. The basis of the sputum consists of thick hyaline mucus stained pink and drops of sero-albuminous exudation stained violet-blue, the relative amounts of these two substances varying in different parts of the film. No trace of fibrin is seen. The cellular elements consist of a few red corpuscles, small alveolar cells, and large endothelial cells exhibiting reticular degeneration, and giving the staining reaction of mucus. The small alveolar cells have the appearance of medium-sized mononuclears or almost of lymphocytes. Macrophages are rare at this stage. Polynuclear leucocytes are very scanty. Pneumococci are found in very small numbers.

Somewhat later, at or about two days before the period of defervescence, in a typical case the sputum becomes less rusty and less viscid, and the microscopic appearances show certain modifications. The hyaline mucus and sero-albuminous exudation are still present, but are less abundant. The same cellular elements are seen, but numerous polynuclear leucocytes now appear. In addition, large networks of fibrillated mucus from the bronchi can be recognized. Microbes are now more plentiful, the pneumococcus often predominating.

A few days later, during convalescence, the sputum having become mucoid or muco-purulent, we find little or no hyaline mucus, no sero-albuminous exudation at all, much mucinous reticulum, mostly derived from the bronchi, numerous alveolar cells often swollen and

pigmented, a relatively large number of polynuclear leucocytes, and many microbes of various sorts.

Comparing the microscopic appearances of the sputum and the pathological changes in the lungs, De Jong points out that the sputum in the early stage corresponds to the stage of engorgement, the drops of sero-albuminous exudation seen in the sputum representing the inflammatory albuminous exudation in the alveoli. Fibrin is generally admitted to be the distinguishing mark of hepatization, and De Jong adds :—

"This notion is so undeniable that authors who have failed to recognize sero-albuminous exudation, hyaline mucus, or the scanty alveolar cells which nevertheless constitute the sputum, have yet described with a certain confidence a fibrinous leucocytic network which has no existence in fact."

Some authors attribute the adhesiveness of the sputum to fibrin, whereas pneumonic sputum contains at the most mere traces of fibrin. What has been described as fibrin is the fibrillated form of mucus or the reticulated appearance presented by cells that have undergone mucous degeneration, whether limited or aggregated into large networks.

Seeing that fibrin is only expectorated in minute traces, why does it remain in the alveoli ? Hanau supposes that the pneumonic sputum comes from alveoli in the stage of engorgement surrounding the area of hepatized lung, not from the hepatized part itself. He considers that the exudation is too adherent to be detached by expectoration, and is only eliminated when resolution sets in. De Jong's view is that the fibrinous exudation remains in the alveoli because it is adherent like the fibrin of a phlebitic clot.

What is expectorated is the cellular elements lying among the fibrinous network, together with the liquid contained in the alveoli. If one gently squeezes in one's fingers a pleuritic fibrinous clot, a few thick drops of albuminous fluid escape. Similarly, the expiratory effort of cough compresses the hepatized lung, and what is expec-

torated is sero-albuminous fluid, representing plasma whose fibrinogen has been precipitated to form fibrin, mixed with hyaline mucus and certain cells.

With respect to the chemistry of hepatized lung, De Jong recalls some experiments of Sotnischewsky [5], a pupil of Hoppe Seyler, who found that watery extracts of red hepatized lung yielded an albuminoid substance that coagulated at a temperature of 54° C., a substance allied to myosin and fibrinogen. This substance could not be obtained from lung in the stage of grey hepatization or from healthy lung. Watery extracts from the two latter coagulated at a temperature of 60-70° C., like certain well-known albuminoids. De Jong suggests that the special albuminoid of red hepatization represents the sero-albuminous fluid found in the sputum in the early stages of pneumonia.

The cause of the adhesiveness of the sputum was studied by Kossel [6]. According to his observations pneumonic sputum contains more nuclein than tuberculous sputum. But although nuclein in solution possesses a consistency and adhesiveness analogous to that of pneumonic sputum, Kossel did not venture to make a positive assertion on this topic. Sahli [7] says that pneumonic sputum is usually very viscid on account of the nuclein it contains. De Jong disagrees with this view, and holds that viscidity of the sputum depends on the thick hyaline variety of mucus.

With regard to the presence of mucin in the sputum, Wanner [8], in opposition to the statements of Renk, finds that pneumonic sputum contains a considerable quantity of this substance, more than is found in tuberculous cases. The same author separated albumin from the other constituents of the sputum and estimated its quantity at different stages. Albumin is very abundant in the early days of pneumonia, but its amount diminishes with the progress of the disease.

In order to test the value of a bacteriological examination of the sputum, Dr. Paul Fildes, assistant bacteri-

ologist to the London Hospital, made a systematic investigation of a certain number of cases at my request. The following is the report which he has been kind enough to furnish :—

*Examination of Sputum from 16 Cases of Lobar Pneumonia.*

The sputum was expectorated into a sputum bottle and examined on the same day. The specimens were collected at dates varying from the third to the fourteenth day of the disease. Each case was examined microscopically and by culture on agar.

Microscopically pneumococci were found in every sputum; in 11, however, they represented a small minority of the organisms present. In two cases the pneumococci were in slight excess, while in three they were practically the only organisms seen.

In culture no pneumococci were demonstrable in six cases, while in three they were present, but overgrown by other microbes. Two cases showed an excess of pneumococci, and in four these were obtained in an almost pure condition. In one case the predominant organism was found to belong to the *M. catarrhalis* group. The other organisms found, in addition to the pneumococcus, were the usual flora of the mouth.

The bacteriological examination of sputum expectorated by a patient suffering from lobar pneumonia appears, therefore, to be an unsatisfactory method of detecting organisms present in the lung; indeed, the one case in another series in which the pneumococcus was found in such numbers and conditions as strongly to imply a pathological multiplication was a case of bronchitis and not lobar pneumonia. No connection was found between the purity of the pneumococci in the sputum and the date of the disease. The inconclusive results are probably in part due to mechanical difficulties in obtaining a specimen direct from the air-passages before it has become contaminated by the secretions of

the mouth. Owing to the tenacity of the sputum this difficulty is very marked in lobar pneumonia.

## Physical Signs

With regard to physical signs I have little to say. The causation of the crepitant râle of Laennec or the fine hair crepitation is still in dispute, an alveolar, bronchiolar, and pleural origin each having its advocates. The practical point is that it is really not an important sign because it is an uncommon one. On the one hand, it is apt to be confounded with the fine crepitation of œdema, and on the other it is often never heard at all in cases carefully watched from the first appearance of physical signs. From its superficial acoustic quality I believe it is only heard when the pneumonic process reaches the surface. A localized deficiency of the breath sounds is a commoner and more valuable sign of commencing pneumonia. Occasionally a slight tympanitic impairment of the percussion note is the first recognizable sign, in which case a layer of relaxed lung may separate a deep-seated focus of consolidation from the chest wall.

Redux crepitus is a sign which is often absent throughout the course of resolving pneumonia, a fact which seems to cast doubts on the alveolar origin of crepitation in general. We know that at this stage liquefaction and absorption of the exudation in the alveoli are in active progress. On the alveolar theory crepitation should be audible now. It seems more probable that redux crepitus is produced in the small bronchi. Lastly, I would emphasize the great value of direct auscultation in doubtful cases. I have often been able to hear faint tubular breathing with the ear applied to the chest wall when I could not hear it with the stethoscope.

## Heart and Blood-pressure.

The fact that most patients die from circulatory failure and not from the direct results of pulmonary consolidation, has long been recognized, and the ominous import of a

rapid, weak pulse is familiar to every practitioner of medicine.

In recent years the application of the sphygmomanometer in cases of pneumonia has given greater precision and more exact expression to this view. Dr. G. A. Gibson [9] writes :—

"It may be stated as a general rule that the pressure tends to be a little below the normal, with considerable fluctuations throughout the course of the disease. It has been asserted that there is a sudden fall at the period of the crisis; this, however, has certainly been far from common in my experience. A pressure, appreciably below the normal in pneumonia, is invariably of evil omen, and any considerable fall bodes disaster. When the arterial pressure expressed in millimetres of mercury does not fall below the pulse-rate, expressed in beats per minute, the fact may be taken as of excellent augury, while the converse is equally true."

These conclusions have received support from the observations of Gordon [10], Hare [11], and Lambert [12].

In a later paper Dr. Gibson [13] supplements his previous remarks as follows :—

"Even in favourable cases there may be a fall of pressure at the crisis of the affection. As a general rule, however, the fall is at once small and brief : in a few hours the pressure rises, at least to the former level, by the balance of the circulation being restored. The only exceptions to the general principles which have been formulated concern the extremes of age. Children have a much lower arterial pressure and a much higher pulse-rate than their seniors, and there may be an apparent discrepancy on this account, unaccompanied by any danger. Elderly people, on the other hand, are very liable to have a higher pressure and a lower rate of pulse than are found among those who are younger; and in such individuals, in spite of the fact that the arterial pressure stands at a higher level than the pulse-rate, there may be imminent danger. The principle,

in its exact and narrow sense, is accordingly only applicable to adults in the prime of life."

Lambert finds that in some young adults with a pulse below 120, and a blood-pressure above 105 during the disease, though there was no change of pressure at the crisis, it fell below 100 after convalescence had set in—that is to say, the pressure was lower during convalescence than during the disease. In others the pulse remained belowed 120, and the pressure below 105, but as soon as the crisis occurred and convalescence set in the pressure quickly rose to 120 to 130. In certain cases in which neither pulse nor temperature was high the blood-pressure remained very low—below 100. Still, Gibson's rule did not point to a bad prognosis, and the patients recovered, a low blood-pressure persisting during a slow convalescence.

Lambert points out that Gibson's rule does not hold good in elderly patients with arterio-sclerosis, and in subjects of chronic nephritis. But while admitting the somewhat variable results of his observations, he expresses his belief that estimations of blood-pressure supply useful data for treatment—a low pressure, for instance, suggesting the undesirability of administering alcohol, strychnine and camphor being more useful in such circumstances.

Observations on the blood-pressure and the pulse-rate made for me by Dr. E. G. Fearnsides, medical registrar, and Mr. H. L. C. Noel, my house physician, confirm Dr. Gibson's conclusions in the main. The blood-pressure was generally rather below the normal; very low pressures—*i.e.*, below 100—being found in children only. In no case was there a sudden fall at the period of the crisis. In several instances there was a gradual lowering of pressure for a day or two before defervescence occurred, the pressure rising again slowly afterwards. The only case in adults in which the blood-pressure was lower than the pulse (blood-pressure 110, pulse 120) died. In another fatal case, however, a young man, aged 26, the blood-pressure remained

higher than the pulse-rate throughout, the last reading being blood-pressure 120, pulse 112.

If we survey the results of *post-mortem* examination of the heart in cases of pneumonia, excluding pericarditis, endocarditis, and the enlargement due to chronic renal disease and emphysema, we cannot fail to be struck by the almost invariable absence of dilatation. The heart-muscle seldom shows any gross disease, though possibly routine examination with the microscope might reveal slight changes resembling those described by Királyfi in guinea-pigs dying frrm pneumococcal infection. The absence of dilatation suggests that the fatal circulatory failure cannot be attributed to insufficiency of the heart's muscle alone, but must in the main depend on exhaustion of the vasomotor centres.

## Œdema.

Cutaneous œdema is a rare occurrence in pneumonia. My attention was directed to this symptom some years ago by the case of a boy 4½ years old, in whom pneumonia terminated by lysis on the thirteenth day. Four days later the temperature rose to 103°, and thereafter oscillated between 101° and 98·8° for some days. On the twenty-second day the face and legs became puffy and œdematous, his aspect suggesting renal dropsy. But the urine, though scanty, remained free from albumin. The dropsy disappeared in three or four days. The chest was explored on the twelfth day, and again on the twenty-third day, with a negative result. Subsequently an empyema was opened and the child recovered.

Fóa [14] seems to have been the first to describe œdema as a result of infection of rabbits with the pneumococcus, and he distinguished two types of this micro-organism, according to its effects—the œdematogenous and the fibrinous. To the first he attributed toxic, to the latter septic properties. The œdema observed was cutaneous and mediastinal. Arullani [15] has more

recently met with a similar result of pneumococcal infection, and came to the conclusion that the œdematous tendency is due to a selective action of the pneumococcus on the blood-vessels, more especially the veins, causing a phlebitis or thrombosis.

Dogliotti [16] reported four clinical cases bearing on the same point, from the service of Dr. Mercandino, of Turin. In a man, aged 60, pneumonia was followed by empyema, and six weeks after the onset œdema appeared on the anterior surface of the trunk and spread over the whole body. In another pneumonic patient, aged 10, empyema developed and was incised. Directly afterwards, the hands, upper arms, face and scrotum became œdematous. In a third case a metapneumonic serous effusion into the pleura was followed by hyperæmia and œdema of the hands and upper arms. In a fourth case, after an attack of pneumonia, incision of a small subcutaneous abscess at the angle of the right scapula was followed by œdema of the dorsum of both hands.

In three of the above cases Dogliotti found that this œdematous fluid was non-inflammatory and contained no pneumococci. In one case, where œdema was limited to the hands, the fluid contained capsulated diplococci. Dogliotti from these facts infers that there are two kinds of metapneumonic œdema : non-inflammatory cutaneous dropsy more or less generalized, of toxic origin, and localized inflammatory œdema excited by the pneumococcus itself.

It is common to find œdema of the lung and mediastinal tissues in fatal cases of pneumonia, both probably in many instances of inflammatory origin. But cutaneous generalized œdema, as in my own case, can hardly be regarded in the same light, and may be a toxic effect of the pneumococcus, as Dogliotti suggested. It is noteworthy that, in all the five cases referred to, œdema developed in the later stages of pneumonia, in three cases it was associated with empyema, in one case with serous pleural effusion.

## Relation to Tuberculosis.

The relation of pneumonia to tuberculosis receives little notice from most writers, and when the question is referred to it is dismissed in a few words. Louis and Walshe seem to have regarded the occurrence of pneumonia in tuberculous lung as not uncommon. Wilson Fox thought it was uncommon, an opinion shared by Aufrecht and by Sturges and Coupland. Sir William Osler says that "pneumonia is a not infrequent complication of chronic phthisis."

In the course of twenty-five years' service on the staff of the Brompton Hospital, during eight of which I held the post of pathologist, I was much impressed with the very rare occurrence of acute lobar pneumonia in tuberculous subjects. I cannot recall a single case observed during life, and in the *post-mortem* room I only met with two or three cases of lobar pneumonia in tuberculous cases which occurred during the great influenza epidemic of 1890. Considering the size of the Brompton Hospital with its 300 beds, most of them occupied by tuberculous patients, it seemed strange that pneumonia should not make its appearance more often. This experience suggested the question whether there was some opposition between the two diseases.

Solidification of the lower lobes of the lungs in advanced tuberculous disease is by no means rare. But such terminal consolidation represents confluent bronchopneumonia, whether tuberculous or resulting from secondary infection with other microbes, and differs entirely from true lobar pneumonia, both clinically and anatomically. The records of necropsies at the London Hospital show that obsolete tuberculous nodules are often found in the lungs in cases of lobar pneumonia. But lobar pneumonia complicating declared and progressive tuberculosis of the lungs is exceedingly rare.

The relations of the two diseases involve the question of secondary infection in pulmonary tuberculosis, which is still *sub judice*. As will be seen in the next lecture,

some French observers hold that benign types of pneumococcal infection are not uncommon in latent forms of pulmonary tuberculosis. But however that may be, acute lobar pneumonia is assuredly most rare in my experience.

## Relation to Rheumatic Fever.

Acute lobar pneumonia complicating rheumatic fever is very uncommon. I venture to give a short account of a very remarkable case which I have previously described in a clinical lecture, in which the two infections seemed to develop simultaneously.

A man, aged 29, was admitted with pain in various joints on June 7. The pain began in the left shoulder on the 1st, and the same night he became hot and feverish, and had cold shivers and sore throat. On admission he was sweating freely; temperature 105·4° F. No fluid was detected in the painful joints. The shoulder was acutely painful on movement. The heart's apex beat was slightly displaced outwards; sounds weak, no murmur; lungs clear. The next day (the 8th) there was pain in the right side; pleuritic rub was heard; 9th: Signs of consolidation in the right lower lobe. The pains in the joints were relieved by salicylates; temperature unaffected, oscillating between 104° and 99°. Signs of fluid appeared at the right base, and he was needled on the 21st, without success. The left shoulder remained very painful and became distinctly swollen. July 5: Urine contained a small quantity of albumin and blood, and a systolic murmur developed in the pulmonary area. After several unsuccessful explorations pus was at last found, and the right pleura was drained. The urine cleared up, the cardiac murmur disappeared, and after a slow convalescence the patient was discharged with a small sinus on October 2. A few weeks later, on his return from a convalescent home, he was looking very well, the sinus had closed, and slight stiffness of the left shoulder alone remained.

This was at first taken for an uncomplicated case of rheumatic fever, though a temperature of 105° F. and a rigor at the onset were unusual. From the history it is clear that if this was a combination of rheumatic fever and pneumonia, as seemed probable, it was a true mixed infection, the two diseases appearing almost, if not quite, simultaneously. How far the persistent arthritis of the left shoulder was rendered septic or infected with the pneumococcus is uncertain.

A further reference to the subject of rheumatism and pneumonia will be made in the next lecture.

## Relation to Influenza.

It seems to be the fact that the pneumonia of influenza is of two kinds : (1) True influenzal pneumonia, the result of the influenza bacillus, which is always broncho-pneumonic ; (2) lobar pneumonia, which is probably always pneumococcal. The first may arise at any stage ; the latter generally appears rather as a sequel than as a substantive part of the influenza, and is to be regarded as a secondary infection.

I wish here to add my testimony to that of Sturges and Coupland that the diagnosis of influenzal pneumonia is often made on very insufficient grounds. There is a tendency to forget that pneumonia, like other infections, may begin with general toxæmic symptoms, lasting some hours or days before any local manifestation can be recognized. I have known otherwise typical cases of pneumonia called influenzal because the early symptoms were of a general febrile character, consisting of headache, lassitude, aching in the limbs, without any evidence of respiratory trouble. Influenza was diagnosed at first, and when pneumonia declared itself subsequently it was styled influenzal.

It is generally admitted that the prognosis in pneumonia supervening on influenza is far more grave than in the primary substantive form of the complaint. Some writers are inclined to account for various deviations

from the normal type on the hypothesis of a concurrent or antecedent influenzal infection. Without denying that this is true in some cases, I believe that the part played by influenza in cases of pneumonia running an anomalous course has been much exaggerated. The more we see of pneumonia the more clearly must we recognize the great variety of its manifestations in individual cases.

Dr. Bulloch states that in recent years it is very rare to find the influenza bacillus in the secretions of cases clinically regarded as influenzal.

## Delayed Resolution.

Resolution of the exudation is generally so rapid and complete that any apparent failure of this process should always be subjected to very close scrutiny. Until exploratory puncture has assured us of the absence of pleural effusion we should hesitate to diagnose delayed resolution. But in exceptional cases resolution may be deferred for weeks or months, and yet the lung may ultimately undergo *restitutio ad integrum*.

In certain seasons resolution may be slower than usual in a considerable proportion of instances, as seemed to me to be the case this winter. It is seldom possible to assign any cause for this delay in resolution. Alcoholism, syphilis, cachectic conditions, destitution and privation, which are commonly given as predisposing causes, are by no means invariable antecedents. Delayed resolution may occur in healthy children and in robust adults. In two cases delayed resolution was associated with acute endocarditis supervening on old endocarditis, which was only disclosed at the necropsy.

A. Fraenkel has stated his belief that delayed resolution is generally the result of fibrosis of the lung. The complete recovery that may ensue in such cases and the clearing up of all physical signs of disease are opposed to this view. In the future radiographic observations will assist the diagnosis in such circumstances.

### Termination in Fibrosis—Organizing Pneumonia.

On this question opinion has been divided. Some authors hold that the pneumonia which is followed by induration is always a special form which differs from the ordinary sthenic type. Others consider that lobar pneumonia of the classical kind may in exceptional instances undergo fibrosis. The first view, which was advocated more especially by Wagner and Heitler, seemed to me to be supported by a case I published some years ago under the title of "Sub-acute Indurative Pneumonia" [17].

Case 1.—In this case, that of a man, aged 44, the illness began with sudden chills, weakness, and cough, but the patient was only confined to bed for two days, though ailing from the first and complaining of cough, expectoration, night sweats, and dyspnœa. Death took place about four months after the onset. The patient had been a drinker.

*Post mortem* the right lung was solid and firm throughout, the upper lobe of pale grey colour, with irregular pigmentation, the lobules being clearly marked out in places. Towards the apex there were two small cavities surrounded by softened lung tissue. The lower lobe was red, granular on section, and softer than the upper lobe. No dilated tubes. Microscopical examination showed fibrinous plugs in the alveoli, surrounded by a delicate capsule of young connective tissue containing scanty capillary blood-vessels. Only very slight interstitial thickening was present. The solid grey lung showed a more advanced condition of the same process, the fibrinous plugs having been almost entirely converted into fibro-cellular tissue containing numerous capillary vessels. The interstitial thickening was more pronounced than in the red parts, but was relatively slight, and the outlines of the alveoli could generally be made out.

I was unable to detect the presence of any microbes myself, but Dr. Turnbull has been kind enough to

examine fresh sections by more modern methods, and reports as follows: "In sections of the red part stained by the Weigert-Gram method, there are a very few distorted Gram-positive bodies which appear to be distorted oval cocci and diplococci. These may be remnants of pneumococci, but there are, unfortunately, no well-formed cocci and diplococci. There is no evidence of other organisms in sections stained by Twort's method. In sections of the grey part stained by the methods of Weigert-Gram and Twort no bacteria are present."

This was a case of "organizing pneumonia," not of the acute sthenic form, which seemed to support the view of Wagner and Heitler that indurative pneumonia is a special form distinct from the acute classical variety. But I met with another case subsequently which led me to modify this opinion.

Case 2.—Pneumonia in a man, aged 43, began suddenly with pain in the side, vomiting, and repeated rigors, followed by cough and expectoration. On admission on the tenth day of the disease the temperature was 104° F.; sputum copious, watery, and frothy. Slight dulness at the base of both lungs, weak breath sounds, and crepitations. On the eleventh day herpes labialis appeared, and the sputum became viscid and rusty, and there were more definite dulness and tubular breathing at the right base. Delirium set in the next day, noisy but not active, and continued till his death. Signs of consolidation spread over the back of the right lung. Temperature varied from 103° F. to 101° F. till the seventeenth day, when it fell to normal, but rose again gradually to 101° F., falling to normal on the twentieth day, and not rising again. Profuse diarrhœa developed the last three or four days, and with increasing delirium and weakness he died on the twenty-first day of the disease.

At the necropsy I found the following conditions on the right side: General fibrinous adhesions, firm and fibrous along the posterior border. Posterior part of all three lobes solid, of dull red colour, on section wet and

glazed, no granulation of surface, interlobular markings distinct, no coarse fibrous band, no dilated bronchi. Anterior margins of both lungs emphysematous. Microscopical examination of the hepatized lung showed practically the same changes as in the red solid portion of the right lung in the first case—viz., organization of the fibrinous alveolar exudation into young connective tissue, but in this case there was no interstitial thickening.

This was clearly a case of severe lobar pneumonia, passing on to fibrous transformation of the lung in the course of three weeks. Here, as in the last case, there were no signs of old fibrosis, the lung showing merely a moderate degree of emphysema.

With the kind permission of my colleague, Dr. F. J. Smith, under whose care the patients were, I am able to give particulars of two more cases, with a pathological report by Dr. H. M. Turnbull, Director of the Pathological Institute of the London Hospital.

Case 3.—The patient, a married woman, aged 48, was admitted under the care of Dr. Smith, on April 9, 1908, with a bed-sore, complaining of cough, shortness of breath, and inability to lie on the left side. The patient, who had suffered from winter cough for many years, had been laid up in bed the last three weeks with "influenza," the illness being accompanied by much cough and night-sweats. The bed-sore started two weeks ago. On admission the patient was very ill and dyspnœic; pulse 102, respirations 26, temperature 98° F. There were physical signs of consolidation of the whole of the right lung, most pronounced over the anterior surface of the upper lobe, and rhonchi over both lungs. The patient died a few hours after admission.

The details of the acute illness are very deficient, but it is very common nowadays to hear pneumonia described as "influenza" when the symptoms and physical signs are not well pronounced. It is probable that the illness was pneumonia, and nothing else, occurring in a bronchitic subject.

*Summary of Necropsy.*—Acute purulent and chronic bronchitis. Broncho-pneumonia in right middle lobe. Organizing croupous pneumonia in right upper lobe. Great emphysema and engorgement in rest of lung. Organizing fibrinous pleurisy on right side. Anthracosis, fibrosis, and swelling of bronchial glands. Slight atheroma of aorta. Wedge-shaped scars in both kidneys. Calcareous gland in mesentery.

*Macroscopic Appearances.*—The right upper lobe was enlarged, solid, and airless. The cut surface was grey in colour ; it was granular in places, but for the most part smooth, gelatinous, and flecked with yellow. It was somewhat tough, and an increase of interstitial tissue was visible in places. Pus could be expressed from the bronchi in many places. The right middle lobe was collapsed and partly infiltrated ; the bronchioles contained pus. The right lower lobe and the left lung were emphysematous and markedly engorged ; a little pus could be expressed from the bronchioles. The right pleura was covered by a layer of fibrin in which vessels were visible.

*Microscopical Appearances.*—Three portions of tissue were removed for examination from the right upper lobe.

(1) The walls of the bronchioles are infiltrated by numerous plasma cells and lymphocytes, and by a few eosinophile leucocytes. Some of the bronchioles contain a few neutrophile leucocytes, red corpuscles, and desquamated epithelial cells. These cells in some cases lie in an albuminous fluid. A few of the respiratory bronchioles contain masses of swollen fibrin. Many of the smaller bronchioles and alveolar passages contain plugs of a vascularized granulation tissue rich in spindle fibroblasts. Enclosed within this granulation tissue there is usually a varying amount of swollen fibrin ; in a very few cases there are no remnants of fibrin. The plugs occupy almost the whole of the lumen ; they are not, however, fused everywhere with the surrounding walls.

Clefts are frequently left between the plug and the wall. In these clefts there are epithelial cells, which lie upon the wall or completely line the cleft.

The great majority of the alveoli are filled by an albuminous fluid, in which there are a few swollen, mononuclear cells, with vacuolated protoplasm, and occasionally a few red corpuscles. The mononuclear cells are evidently epithelial. A few alveoli contain a network of fine filaments of fibrin. A few contain swollen fibrin. The swollen fibrin is usually invaded to a greater or less degree by granulation tissue. The masses of fibrin are invaded from their periphery. These organizing masses of fibrin are attached in places only to the alveolar walls, clefts being left between the mass and the walls. In these clefts there are usually epithelial cells. The organization of the fibrin in the alveoli is less advanced than in the small bronchioles and respiratory passages. The capillaries in the alveolar walls contain red corpuscles. Very few of the alveolar walls show any sign of thickening. The septa are broadened. This is chiefly the result of œdema, but there is a slight proliferation of fibroblasts and infiltration by lymphocytes and plasma cells.

In sections stained by the methods of Twort and Weigert-Gram, a few Gram-positive diplococci are occasionally present in the fibrin, in the desquamated epithelial cells, and in the lumen of some bronchioles. These organisms are almost all intracellular. They may be pneumococci, but typical lanceolate forms are not present. In one bronchiole there are a few very large Gram-positive cocci and diplococci.

(2) This section is very similar to the first. Organization is, however, more extensive and a little more advanced. The appearances suggest, even more strongly than those of the previous section, that the granulation tissue starts chiefly from one part of the wall of a small bronchiole and extends along the surface of plugs of fibrin which have retracted from the walls of the respiratory passages and infundibula. Granulation tissue does, however, sprout in places from the alveolar walls.

Some of the alveolar walls, particularly those adjacent to septa, are thickened by a proliferation of fibroblasts. A lymphatic in one septum contains a plug of granulation tissue.

The pleura is covered by fibrin, into which pass fibroblasts and capillaries.

There are intracellular Gram-positive cocci and diplococci within some of the masses of fibrin, and in a very few of the plugs of granulation tissue. The cocci are not of typical lanceolate shape.

(3) This section is very similar to the second. Some of the bronchioles are, however, filled by leucocytes; their epithelial lining is partly desquamated. Further, the organization is in general more advanced, remnants of swollen fibrin rarely being present within the plugs of granulation tissue. A large lymphatic in a septum is filled by fibrin, and this is undergoing organization from the periphery.

No organisms are present in the purulent bronchioles. In the rest of the lung there are few cells containing Gram-positive cocci and diplococci. These resemble the cocci in the previous sections, but a few are of lanceolate shape.

CASE 4.—The patient, a man, aged 42, was admitted under the care of Dr. F. J. Smith, on May 12, 1908. The patient, a temperate man, who had suffered from winter cough, began to feel "weak and careless about everything" for five or six weeks. On May 5 he had a sudden attack of pain in the side, and next day became jaundiced. Delirium followed shortly, the patient being unable to give any further account of his illness. On admission on May 12, the eighth day of the disease, he was jaundiced and delirious. Pulse 128, respiration 48, temperature 103° F. Signs of consolidation of the lower lobe of the right lung, which gradually involved the whole lung. Temperature was irregular, varying from 103° F. to 100° F. until the last two days of life, when it fell to 99° F. Death took place on May 24, the twentieth day of the disease.

*Summary of Necropsy.*—Pulmonary embolism, subacute pyæmia, subacute, embolic, focal nephritis in both kidneys. Large red thrombus in left pulmonary artery. Organizing croupous pneumonia in posterior and lower part of upper lobe, and posterior part of lower lobe of right lung; œdema of remainder of right upper lobe; abscesses in right upper lobe; great congestion and emphysema of left lung. Organizing fibrinous pleurisy, right, with focal empyemata between adherent upper and lower lobes. Small calcareous nodule in bronchial gland in hilum of right lung. Great distension, but no muscular hypertrophy of colon; stercoral ulceration of transverse and descending colon; no obstruction in colon or rectum; single diverticulum in descending colon. No thrombosis of large veins of head, trunk, or limbs.

*Macroscopic Appearances of Lung.*—The posterior and lower part of the upper lobe, and the posterior part of the lower lobe of the right lung felt solid. The cut surface of the solid portions were red, moist, and only slightly granular. It was flecked with small yellow dots. It felt firm, but could be broken with little difficulty. In the upper lobe of the right lung there were three or four abscesses about the size of peas. The pleura over the right lung was covered by fibrin, which was partly organized and vascularized. Between the adherent upper and lower lobes there were some small collections of pus.

*Microscopic Appearances (the Upper Lobe of the Right Lung).*—In two lobules the alveoli are distended by thin, albuminous fluid, in which there are a few red corpuscles and a considerable number of greatly swollen, vacuolated mononuclear cells. A few alveoli contain fibrin which is undergoing organization. A bronchiole is present in one lobule, and is almost completely filled by a plug of vascularized granulation tissue. Its wall is considerably infiltrated by plasma cells and lymphocytes.

In the other lobules some larger bronchioles contain a few red corpuscles and leucocytes; their walls are

infiltrated by lymphocytes and plasma cells. The remaining bronchioles, respiratory passages, and infundibula are almost all occupied by plugs of vascularized granulation tissue, or by plugs of fibrin, which are invaded to a greater or less extent by granulation tissue. The completeness of the organization varies in different places; in general it is advanced, the fibrin as a rule having been completely replaced. The plugs are only connected at intervals with the walls of the spaces in which they lie. Thickening of the alveolar walls is rare, and there are little thickening and infiltration of the septa. Some of the septal lymphatics contain fibrin which is undergoing organization.

There are small abscesses, represented by areas in which the pulmonary tissue is destroyed, and is occupied by masses of polymorphonuclear leucocytes. The form of these abscesses and their relation to small pulmonary arteries suggest that they have arisen in alveolar bronchioles.

The pleura is covered by vascularized granulation tissue, in which there are enclosed portions of swollen fibrin.

Neither Gram-positive nor Gram-negative bacteria could be demonstrated in the lung and kidney.

Marchiafava [18], in a paper on "Pneumonia Productiva Resulting from Acute Lobar Pneumonia," discusses this question. In 1884 he described nine cases of this condition, and since then he has observed thirty-two more, all preceded by acute pneumonia and followed by necropsy, in addition to many ending in recovery or in death without necropsy. The upper lobe was affected in eighteen, the lower in fourteen, and the illness lasted for eighteen to sixty-five days from the onset of the acute pneumonia. In twenty-eight of them complications (pulmonary, cardiac, renal, intestinal, meningeal, &c.) were present, and in these the diplococcus, or the diplococcus associated with pyogenic cocci, was often demonstrated.

The naked-eye and microscopical characters described by him do not differ in essential points from those found in the cases already described, organization of the alveolar exudation being the prevailing change. Marchiafava notes that the failure of resolution in such cases occurs oftenest in debilitated or alcoholic subjects, and depends upon failure in the autolysis and absorption of the exudation.

Clinically the condition manifests itself usually by the occurrence of a pseudo-crisis in the attack of pneumonia, followed either by slow resolution or fibrosis, extending over many weeks or months, and recovery, or by death, with or without complications. Persistent hæmoptysis often occurs early. The physical signs may suggest either consolidation or pleural effusion, according as the bronchioles are occluded or not. More or less fever is habitually seen. Complications are the rule in "productive" pneumonia — lobar pneumonia, pulmonary abscesses, pulmonary tuberculosis, empyema and phlegmonous laryngitis, acute ulcerative endocarditis, embolism, purulent meningitis. Marchiafava thinks that this indurative form of pneumonia is not nearly so rare as complication of lobar pneumonia as is commonly believed. It is rarely followed by bronchiectasis, unless it was preceded by whooping-cough or measles, and so may lead to a form of pulmonary fibrosis that is not particularly injurious to the patient. On the other hand, it may give rise to progressive marasmus and death, without the occurrence of complications. Marchiafava's collection of cases is remarkable, and would seem to show that this outcome of acute pneumonia is far less uncommon in Italy than in England. Dr. Turnbull informs me that in 5,400 recent necropsies at the London Hospital, in the years 1907-11, he has only met with two cases of organizing pneumonia among 140 cases of pneumonia.

Dr. J. Fawcett, in his article on "Chronic Interstitial Pneumonia" [19], seems to throw doubt on the origin of

fibrosis of the lung in acute lobar pneumonia. He states that in the Guy's Hospital series of cases there is no case which can be declared as undoubtedly belonging to this group. For although, he says, we must admit that a chronic lobar pneumonia may follow the acute attack, the rarity of this sequence of events is extreme, and indeed in Charcot's case it is almost impossible to deny the pre-existence of chronic disease upon which a more or less acute inflammatory process has supervened.

While fully admitting the rarity of this sequence of events, I am persuaded that it does occur, and in all the four cases I have described it is impossible to affirm the pre-existence of chronic disease of the lung, excluding some degree of emphysema. The process consists in a gradual fibrosis of pre-existing fibrinous exudation into the alveoli. In Cases 2, 3 and 4, the duration of the acute attack did not exceed three weeks, and the fibrinous exudation was already undergoing a fibrous transformation or organization. As to the nature of Case 1 there is more doubt. It certainly was not a sthenic form of pneumonia; possibly it represented an anomalous form of pneumococcal infection, and so was closely allied to the more acute cases. The best name for this class of case is "organising pneumonia," given to it, I believe, originally, by Orth.

The cause of the organization has not been satisfactorily explained. Marchiafava attributes it to imperfect autolysis and absorption of the exudation, which is only another way of saying that it is due to imperfect resolution. But inasmuch as the lung may remain unresolved for weeks or months without any development of fibrosis, clearly some other influence must be at work.

Such cases as those cited by Dr. Fawcett are of a different nature, being insidious and essentially chronic from the first. These are far less rare than the first, and I have met with several instances.

Pneumonia terminating in organization seems to fall into two groups. (1) Progressive febrile cases, with or

without a temporary remission of fever, ending fatally in a few weeks or months. Pulmonary abscesses, gangrene and other complications may arise. (2) Cases where the fever declines by lysis, delayed resolution being succeeded by gradual fibrosis and recovery. I have met with no undoubted instance of this class.

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## LECTURE III.

Mr. President, Fellows, and Gentlemen,—In my third and last lecture I propose to consider the varieties of lobar pneumonia. The typical pneumonia of the text-books is a very striking and interesting disease. But how few pneumonic patients exhibit the classical assemblage of symptoms! Whether we have regard to the mode of onset, the type of fever, the physical signs, the relative predominance of various symptoms, or the duration of the process and its termination, we meet with a considerable proportion of cases which present unusual features.

There has been a tendency among writers to erect a group of atypical pneumonias, including among them such varieties as wandering, epidemic, bilious, infectious, asthenic, typhoid pneumonia. These forms differ from the ordinary disease in many particulars which are met with in varying combinations: albuminuria, enlargement of the spleen, jaundice, insidious onset, severe cerebral symptoms. But Weichselbaum [1] states that the assumption of some clinical physicians that these forms are due to different bacteria is not justified, for the pneumococcus has been found in such cases by various observers, such as Kutschera, Lanz, Maleschini. Kolle and Hetsch [2] also express the opinion that such cases are generally due to the pneumococcus, which is found in pure culture. They consider that the anomalous character of the disease is partly attributable to varying degrees of virulence of the germ, and partly to the reaction of the individual patient. In their experience a careful study of the strains of pneumococci cultivated from such cases sometimes reveals morphological, cultural, and pathogenic characters differing from the normal type.

Further bacteriological investigation is needed before a scientific classification of these varieties of pneumonia can be formulated.

It is not necessary now to insist on the fact, well known to clinical medicine, that many of these irregular pneumonias occur in old people, insane, alcoholic, and renal patients, and in various cachetic states in which the reaction of the organism is obviously greatly modified. That in many instances the part played by the infected organism is decisive as to the course of the infection cannot be doubted.

Although the evidence that lobar pneumonia in the great majority of cases is due to the pneumococcus is conclusive, it seems certain that similar lesions may be produced by other micro-organisms—*Bacillus tuberculosis*, *B. pneumoniæ* (Friedländer), *Streptococcus pyogenes*, and possibly *B. typhosus*, *B. coli*, and *Staphylococcus pyogenes*. Amongst these, the *B. pneumoniæ* (Friedländer) and the *S. pyogenes* will receive special mention.

## "Friedländer" Pneumonia.

This form appears to have attracted little attention in England, but German literature contains a considerable number of publications on the subject. Some important papers have appeared recently, from which I have gleaned much information.

Apelt [3], in 1908, gave a description of ten cases, two of which had been under his own observation, with a review of the more important literature. From this it appears that Philippi [4], in 1902, was the first to describe a case in which Friedländer's bacillus was found during life in the sputum and blood, as well as in the lung, spleen, and bone marrow after death. Lenhartz [5] also described a case in which the same bacillus was found in the blood during life.

Stühlern [6] collected forty-five cases from the literature, in ten of which there was a mixed infection with staphy-

lococci, streptococci, or pneumococci. He added ten cases of his own, in four of which the pneumobacillus was present in pure culture. He states the opinion that the so-called "Friedländer" pneumonia, from the anatomical, clinical, and bacteriological standpoint, may be described as an atypical form of pneumonia. It differs from the genuine form in the great formation of mucus in the infiltration depending on the luxuriant growth of capsulated bacilli and in the imperfect development of red hepatization. A malignant course tending to early death and an absence of herpes are marked clinical features. The pneumobacillus is the predominant organism, and may be the only one present. From these factors he draws the conclusion that this form of pneumonia is a specific infection by the pneumobacillus.

Kokawa [7] made an extensive study of the pathological anatomy of eighteen cases in which Friedländer's bacillus was found in the lungs. From this research he finds that the pulmonary lesion may be lobar or lobular. The surface of the section of the infiltrated lung is extraordinarily slimy, owing to the abundant mucoid material present in the capsulated bacilli. The contents of the alveoli in the early stages consist mainly of pneumobacilli, with some desquamated alveolar epithelium, red-blood corpuscles, and leucocytes. Later on the leucocytes become more numerous, and exhibit many vacuoles due to the formation of mucus excited by the ingested pneumobacilli. The absence of marked fibrinous exudation and hæmorrhage is noted both by Kokawa and by Stühlern, the diseased lung resembling grey, rather than red, hepatization.

Stühlern drew attention to the tendency of the pneumonic lung to undergo suppuration and softening, but Kokawa makes no mention of this. The latter observer agrees with Stühlern in regarding "Friedländer" pneumonia as a definite and specific form; for though in most of the cases the infection is a mixed one, in some instances the pneumobacillus was the only microbe

present. In a later research [8] Kokawa found that intratracheal injections of secretions from the lung containing Friedländer's bacillus in pure culture failed to produce any results in rabbits, except when direct injury was inflicted on the lung, or when the animal was artificially cooled down previously. In these circumstances he succeeded in producing pulmonary consolidation in all respects like that characteristic of "Friedländer" pneumonia in man.

*Account of Recorded Cases.*

A brief account of some of the cases described by Apelt may now be given.

Case 1.—A labourer, aged 42, of alcoholic habits, was seized at night with shivering and malaise. Next day cough and feeling of illness followed. On the third day he was admitted to hospital in a somnolent condition, with a pulse of 140, and signs of pneumonia of the right middle and lower lobes. Blood (15 c.c.) was removed from a vein, and cultivated on agar plates. The patient died five hours after admission. The cultivation of the blood in twenty hours gave abundant growth in pure culture of capsulated Friedländer's bacillus.

*Post mortem* there was greyish-black hepatization of the right middle and lower lobes. The cut surface showed a peculiar slimy, shining appearance, and was bathed in thick stringy secretion. The central part of the lower lobe was in a state of softening. Pure cultures of the pneumobacillus were obtained from the lung, including the softened area, from the spleen, bone marrow, bile, and blood.

Case 2.—A labourer, aged 46, admitted on account of fever, cough, and pain in the chest. Sputum reddish, mucoid, no tubercle bacilli, numerous capsulated pneumobacilli. Signs of pneumonia in right middle and lower lobes. Pulse 120, soft; blood-pressure 75 mm.; heart slightly dilated. On the second day of illness blood from the arm was cultivated. In twenty hours

plates were studded with colonies of Friedländer's bacillus. On the fourth day collapse ensued. The blood-pressure fell to 45 mm. ten minutes before death.

*Post mortem* the right middle and lower lobes were in a state of firm greyish-black hepatization, the section showing a glistening, slimy appearance. Much stringy secretion; no tuberculosis. Pneumobacillus obtained in pure culture from lung, bile, spleen, blood, and bone marrow.

CASE 5.—Labourer, aged 30, admitted under Professor Lenhartz. Three days before admission was taken ill with rigor and pain in left side. Temperature 101° F.; pulse 108, soft. Sputum reddish, slimy and offensive, containing elastic fibres; pneumobacilli in pure culture. On the fourth day blood (20 c.c.) withdrawn from the arm and cultivated, but remained sterile. Physical examination disclosed consolidation of the lower part of the left upper lobe, and X-ray examination confirmed this. On the same day after resection of seventh and ninth ribs a large cavity was opened surrounded by solid lung. The cavity contained blood-stained mucoid pus and small sloughs of lung tissue. On changing the dressings next day the discharge contained long, yellowish, mucoid strings as thick as a cedar pencil. From this fluid an abundant, thick, slimy growth of Friedländer's bacilli was obtained on blood-agar plates. Cultivations from the patient's blood on three subsequent occasions gave negative result. On the eleventh day after operation the temperature fell to normal, the cavity began to contract, and the discharge diminished. But ten days later a fresh attack of pneumonia of the left upper lobe developed, and pneumobacilli were again found in the discharge from the wound and in the sputum. The patient died on the twenty-third day after the operation from heart failure.

*Post-mortem* there was croupous pneumonia of the left upper lobe, with a healing gangrenous cavity in the left lower lobe. Heart muscle fatty. Friedländer's bacilli in

pure culture obtained from the blood and from the bone marrow.

Buxbaum [9] subsequently published two cases of "Friedländer" pneumonia in 1909. In the first, a female. aged 60, the disease began with slight shivering and moderate fever. On the third day signs of pneumonia of the right upper lobe appeared. Herpes was present. Sputum, tenacious, frothy, of rusty colour, contained Friedländer's bacilli, but no pneumococci, tubercle bacilli, or other microbes. Pure cultures of pneumobacilli were obtained. Gradual improvement set in during the third week, and in five weeks the patient had recovered.

In the second case, a man, aged 50, the subject of old mitral disease and scoliosis, the disease began insidiously with repeated slight shiverings and cough. Pneumonia of the right lower lobe developed. Sputum scanty, mucoid, containing various microbes. On cultivation a growth of streptococci and pneumobacilli appeared. Course very slow ; gradual recovery in seven weeks.

In December of last year a very important and interesting case was published by Toeniessen [10]. A man, aged 55, was suddenly taken ill with shivering and pain in the right side ; next day cough and scanty yellowish sputum. On admission on the fourth day of illness the patient did not look ill and the temperature was not raised. At the apex of the right upper lobe there was slight "tympanitic dulness," but no other signs ; sputum scanty and mucoid. The urine was slightly albuminous. The next day the temperature was 102° F., the physical signs had increased, and the patient looked ill. On the seventh day herpes labialis appeared. The sputum was abundant, viscid, brownish red ; numerous non-capsulated diplococci, and large rods with thick capsules were present. A mouse was inoculated with the sputum, and a pure culture of Friedländer's bacilli was obtained. Examination of the patient's blood gave negative result. The consolidation of the lung gradually increased and spread to the lower lobe. The temperature remained moderately

raised throughout. On the twenty-first day X-ray examination which had previously corroborated the existence of consolidation, now showed a marked clearing of the shadow. Pneumothorax was excluded by the physical signs, and an abscess was thought of. But against this idea was the moderate degree of fever, together with the improved condition of the patient. No puncture of the chest was made for fear of infecting the blood with the pneumobacilli. The general improvement continued, the temperature remaining slightly below 100° F. until the twenty-eighth day. On this day, while taking a bath the patient succumbed to a sudden fainting attack.

*Post mortem.*—The upper lobe of the right lung contained a huge cavity, in which was a large slough of lung tissue attached to the wall at one spot. In addition there was much blood-stained fluid, with a peculiar rancid odour. The surrounding lung tissue was solidified. The fluid from the cavity contained Friedländer's bacilli.

Apelt quotes E. Fraenkel's *post-mortem* statistics of seventy-seven cases of pneumonia bacteriologically examined in the year 1907. Of these, sixty were due to the pneumococcus, ten to *Streptococcus mucosus*, and in seven the presence of the Friedländer bacillus was ascertained. Of these seven cases, there was a mixed infection with the pneumococcus in four, with *Bacillus coli* in one, leaving two cases of pure "Friedländer" pneumonia.

### *Conclusions in regard to "Friedländer" Pneumonia.*

The illustrative cases that have been quoted justify certain conclusions, most of which are emphasized by Apelt, Buxbaum, and Toeniessen. Pneumonia of lobar dimensions may be caused by the pneumobacillus alone, as Weichselbaum has always maintained. The typical bacilli may be found in the sputum and in the blood during life, and they have been present in the contents of a pulmonary abscess incised by the surgeon. The appearances of the consolidated lung are not always

fully described, but where a detailed account is given—as by Stühlern and Kokawa more particularly—the hepatization is said to be grey or blackish-grey, and not granular. In most cases the thick, slimy nature of the fluid exuding from the cut surface is specially noted. In one case of Apelt's, where the hepatization is described as red, there was a mixed infection with the pneumococcus. However, in another case of the same series, one of pure Friedländer infection, the hepatization was partly red and partly grey, so that possibly a stage of red hepatization may be passed through. The contents of the alveoli consist mainly of desquamated epithelial cells and bacilli, with very little fibrin and with less leucocytes and red corpuscles than in pneumococcal cases. The tendency to necrosis and suppuration is remarkable, contrasting strongly in this respect with pneumococcal pneumonia. Toeniessen states that suppurative softening occurred in nearly one half of all the cases recorded. In many cases where gangrene and abscess occurred the pneumobacillus alone was present.

With regard to the clinical aspects, most writers are agreed that the course is severe and the mortality is terribly high. Apelt goes so far as to say that he believes that only one recovery has been recorded—viz., one in which Lenhartz drained a gangrenous cavity in the lung. Buxbaum, however, points out that of the ten cases recorded by Stühlern, three recovered, and both of his own cases made a good recovery. In Wiens's series of 33 cases of pneumonia, one due to the Friedländer bacillus recovered. Nevertheless, it is clear that Friedländer pneumonia is a severe disease. The patients are nearly always gravely ill from the first. In three cases of Apelt's death took place on the third day from toxæmia. In two of the same observer's cases pneumobacilli were found in the blood on the second and third day respectively. In other cases cultivation of the blood gave a negative result. The extremely high mortality is attributed to the rapid flooding of the blood with the

bacilli. An initial rigor and herpes labialis are said to be uncommon, but these seem to have been noted in a fair number of cases. The fever is variable—irregular in many cases, of high remittent type in others. There was a crisis in one case only. The diagnosis depends on the detection of Friedländer bacilli in the sputum and blood.

The development of gangrene or abscess in a case of pneumonia should direct attention to the possibility of the case being one of "Friedländer" pneumonia, and cultures of the sputum and blood should be made. The recognition of the bacilli in the sputum is easy, but their detection in the blood is not always possible.

The prognostic significance of bacteriæmia in this disease is considered to be very grave by Apelt. Most cases with bacilli in the blood die, and those that recover are unusually severe. But in one of Wiens's cases bacilli were found in the blood and the disease ran a mild course. Buxbaum raises the question, without attempting to answer it, whether the malignant forms of pneumonia are related to Friedländer infection, or whether they are dependent on mixed infection? It appears to be a fact that the most malignant fatal cases may be solely due to the pneumobacillus, to mixed infection with this microbe and others, or to the pneumococcus alone.

Toeniessen considers that in mixed pneumococcal and Friedländer infection, the latter being the more resistant organism, overpowers the pneumococcus. This is shown by consecutive observations in cases where several varieties of microbes were present at first, but ultimately the pneumobacillus alone was found. Experiments with simultaneous injections of mixed cultures of Friedländer bacilli and pneumococci confirmed this view, for on the second passage through an animal the Friedländer bacillus was present in pure culture.

Further light was thrown on some of the peculiarities of this infection by Toeniessen's experiments. The comparatively low temperature of the patients in many cases,

as compared with pneumococcal infection, is explained not so much by the special action of the bacillus as by the massive flooding of the body with bacterial substances. Injections of cultures into rabbits and guinea-pigs cause at first high fever, which is soon followed by collapse temperature if the dose injected be large; whereas the result of small doses is to cause a high temperature which lasts for several days. The relatively low temperature observed in localized infections with the pneumobacillus is explained by the slight local reaction, setting free small quantities of bacterial substances for absorption.

The persistent infiltration of the lung and the continued discharge of virulent bacilli, which lasted for eight weeks in one case, are attributed to the highly resistant character of the bacilli and to the relatively slight local reaction induced. He compares with this the behaviour of the pneumococcus, which maintains its virulence for a few days only while the infiltration is extending, and excites an intense leucocytosis in the inflamed area. Pneumococcal cultures injected into the peritoneal cavity of animals give rise to a marked fibrino-purulent exudation with meteorism depending on intestinal paralysis. Cultures of Friedländer's bacillus, on the other hand, provoke an exudation poor in pus-cells, consisting mainly of capsulated bacilli.

*Notes of a Case of Friedländer Pneumonia.*

The following is the only instance of "Friedländer" pneumonia that I am able to cite from the records of the London Hospital. Dr. Turnbull, who made the *post-mortem* examination, has kindly supplied me with a description of the case.

The patient, an army pensioner, was admitted to hospital on August 19, 1910, under my colleague, Mr. H. M. Rigby, who kindly allows me to use the case. On admission the patient was suffering from stricture of the urethra, and had a temperature of 101·8° F. Fifty

ounces of foul alkaline urine were removed by catheter, and the temperature fell next day to 99° F. Much difficulty of micturition persisted. Four days later the temperature rose to 102·7° F., and slowly fell again in two days to 100° F. On August 23 the temperature fell to 96° F., and death ensued. The pulse varied from 108 to 116, the respiration from 20 to 24 throughout.

*Summary of Necropsy.*—Croupous pneumonia (Friedländer's); ascending pyelonephritis. Early red hepatization of lower lobe of right lung with great œdema; œdema and emphysema of rest of lungs; fibrinous pleurisy (right); stricture of urethra with sinus leading into perineal abscess; diphtheroid cystitis; inflammation of pelves of kidneys; a few hæmorrhagic and purulent streaks in kidneys, especially the right kidney, &c.

The whole lower lobe of the right lung was swollen, dark in colour, and felt solid and boggy. The pleural surface was covered by a thin layer of fibrin. Serosanguineous fluid flowed from the cut surface spontaneously. The cut surface was of a deep-red colour, with no visible aeration. It was slightly granular in places. Plugs of fibrin could be expressed from some of the bronchioles. The appearance resembled that of the early stage of red hepatization in an ordinary lobar pneumonia.

*Microscopic Appearances: Section from Right Lower Lobe.*—The alveolar capillaries are engorged. The larger bronchioles contain a little fibrin, in which are entangled some leucocytes and red corpuscles. Bacilli are visible therein, even in the hæmatoxylin and eosin sections. Many of the respiratory bronchioles and alveolar passages are conspicuous, owing to their containing masses of bacilli in addition to leucocytes. The infundibula are filled by albuminous fluid, fibrin, red corpuscles, polymorphonuclear leucocytes, and bacilli. The relative amount of these constituents varies. A large number of infundibula contain fibrin, but the fibrin is present in fine filaments and the filaments are not abundant.

Red corpuscles are very numerous. There is relatively little infiltration by leucocytes. Bacilli are very numerous and are conspicuous in the hæmatoxylin and eosin sections. The organisms are Gram-negative; the majority are short, stout, almost oval, diplobacilli. Coccal and longer bacillary forms are also present. They appear to be encapsulated. Large numbers are intracellular. Gram-positive organisms are not present. The picture is that of early, red hepatization with an extraordinary number of Gram-negative bacilli which have the morphological characters of Friedländer's pneumobacilli. No cultures were made.

Friedländer pneumonia is evidently a rare disease. From the cases recorded it appears that although the hepatized lung usually presents a peculiar slimy surface on section this is not invariably the case, and the consolidation may even be red and somewhat granular. It is probable, therefore, that cases of this disease may escape recognition even on the *post-mortem* table. If the sputum of every case of pneumonia were examined bacteriologically this mistake would be less likely to occur.

### Streptococcal Pneumonia.

The accounts of this form are scarce. Weichselbaum refers to cases of this description, without giving details, and states that streptococcal pneumonia is at times indistinguishable from typical lobar pneumonia, and also that in some pneumonias clinically regarded as anomalous cocci are found closely resembling *S. pyogenes*, both microscopically and culturally.

Filaretow [11] published four cases which appear to have been of broncho-pneumonic type. The leading features described are intermittent fever and a prolonged course, lasting as much as one to two months. In one case a subacute streptococcal pneumonia supervened on acute fibrinous pneumonia during the stage of resolution. All four cases recovered. In the same journal a very brief abstract is given of a paper by A. Lewin on the same

subject. Intermittent fever, repeated rigors and sweats were the prominent symptoms, and the physical signs were those of broncho-pneumonia.

More recently, Schottmüller [12] described six cases of lobar pneumonia due to *S. mucosus*, which was found in the blood in every instance, and in the spleen and bone marrow as well as the lung in five cases that ended fatally. The pneumonia in these cases seemed indistinguishable from the ordinary pneumococcal variety, beginning with a rigor or pleuritic pain as a rule, and being associated wth herpes in some instances.

### Pulmonary Congestion.

In Lippmann's [13] monograph reference is made to researches on certain affections styled "pulmonary congestion" by French authors, which in this country are regarded as varieties of pneumonia. These include "maladie de Woillez," an abortive form of pneumonia, pleuro-pulmonary congestion of Potain, a variety of pleuro-pneumonia, and the spleno-pneumonia of Grancher, of which a further account will be given later on. Carrière made a bacteriological examination of ten cases of "maladie de Woillez" by the method of direct puncture of the lung. In two cases the result was negative. In eight cases culture revealed the presence of the pneumococcus; in four the culture was pure; in the remaining four staphylococci or streptococci were present also. Inoculation of rabbits did not prove fatal in any case. Carrière concluded that this affection is due to various microbes, the pneumococcus being the usual cause. The disease is generally due to the localization in the lung of pneumococci of attenuated virulence.

Roux, in his thesis in 1899 on pneumococcal congestion of the lung, stated that the pneumococcus may cause "maladie de Woillez," pleuro-pneumonia, congestion, or splenopneumonia. In such cases the microbe possesses an attenuated virulence, and recovery is the rule. Grasset, in his lectures, includes "maladie de Woillez," abortive

pneumonia, pneumonic febricula of Charcot and Bernheim, and pleuro-pulmonary congestion under the comprehensive term "pneumococcie thoracique atténuée."

Caussade and Laubry brought forward a case of "massive congestion of the lung" simulating a large pleural effusion, which lasted three and a half months. The pneumococcus found in the sputum proved fatal to mice in eighteen hours, and the virulence was maintained throughout the course of the disease. In the discussion that followed the reading of this paper Rendu stated that in his hands puncture of the lung in cases of pulmonary congestion always yielded a virulent pneumococcus when the result was positive. In his opinion, instead of postulating a scale of pneumococci of varying virulence it was more rational to admit that it was the vital reaction of the individual and his degree of resistance which gave rise to the different clinical varieties. Hirtz reported a case of pulmonary congestion which was noteworthy on account of the abundant purulent expectoration, which contained the pneumococcus in pure culture.

## Splenopneumonia.

The term "splenopneumonia" was introduced by Grancher [14] in 1883 to denote "a variety of subacute pneumonia which simulates pleurisy with moderate effusion." Grancher, in his original account, described three cases of this complaint. In these the onset was attended with pleuritic pains and shivering. The physical signs indicated, in his opinion, pulmonary congestion and a small pleural effusion, the physical signs being dulness on percussion, diminished vocal fremitus, weak blowing breathing, broncho-ægophony. All the cases made a slow recovery in the course of some weeks. Grancher believes that these cases are examples of splenization, in which the solid lung is red and smooth. Microscopically the alveoli are filled with epithelial cells and sero-albuminous fluid. The contents of the alveoli seemed to him to account for the physical signs. Grancher did not

express any opinion as to the etiology of splenopneumonia, but considered that the prognosis was less favourable than in simple pleurisy and pulmonary congestion.

Mosny and Malloizel [15], in a recent article, remark that the designation splenopneumonia has been applied by subsequent French authors to various kinds of pneumonia, among which may be mentioned wandering, influenzal, typhoid, and rheumatic pneumonia. Bacteriological investigations of similar cases by Alfaro, Caussade, Chantemesse, Gallois, have revealed the presence of pneumococci and of the "habitual parasites" of the lung.

Mosny and Malloizel point out that the pathological anatomy of the disease is somewhat ill-defined, as the patients usually recover. No general agreement exists as to what is understood by splenopneumonia. The tendency has been to regard as splenopneumonia any pseudo-pleuritic affections of any kind, whether primitive or secondary to some other infection. The authors regard splenopneumonia as a clinical syndrome depending on different causes, and they include under this head all cases in which, without notable pleural effusion, there are pleuro-cortical lesions and signs of pleurisy well or ill-defined. In every splenopneumonia there is a subpleural or cortical consolidation, with a corresponding pleural lesion characterized by œdema and a trifling exudation. The affection is often bilateral. Diagnosis is much facilitated by puncture with a syringe and withdrawal of fluid from the pleural cavity or from the œdematous pleura. The cytology of the fluid obtained gives no information as to etiology, but supplies proof of the existence of pleuro-cortical lesions—viz., large hyaline cells (macrophages), some of irregular shape, occasionally phagocytic, and at times polynuclear leucocytes and lymphocytes. In some instances puncture obtains only a few drops of turbid fluid, "pneumonic pseudo-pus," especially in cases regarded as pneumococcal from the bacteriological and clinical standpoint.

Splenopneumonia may begin with shivering, pain in the side, or symptoms of a common cold. At times the onset is insidious. Herpes labialis is not uncommon. Whatever its cause may be, its tendency is always towards recovery.

Though the authors disclaim the intention of making a strict etiological classification, they divide cases of splenopneumonia into four groups.

(1) *Simple Transitory Attacks accompanied by Acute Bronchitis.*—In these cases the pneumococcus is very often found in the sputum. Similar ephemeral attacks may occur in tuberculous subjects.

(2) *Pulmonary Congestions due to the Pneumococcus or Similar Microbes of greater Severity and more Persistent.*—Various forms may be distinguished according to the relative preponderance of pleural or pulmonary inflammation. This group includes "maladie de Woillez," pleuro-pulmonary congestion, and cases lasting several weeks like those described by Grancher. In such cases the pneumococcus may be found in the sputum or in the blood withdrawn from the lung, but the authors consider that the pneumococcal infection in many cases of Grancher's type is secondary to a latent tuberculosis. Splenopneumonia may also be caused by septicæmia of various kinds, typhoid fever, and influenza. In the case of influenza it is apt to assume a serpiginous form.

(3) *Rheumatic.*—Splenopneumonia is said to be common in rheumatic fever, though often slight and unrecognized, appearing and disappearing rapidly. Successive attacks are not uncommon. Pain is seldom a marked feature. The attacks are always febrile. The authors state that the supervention of pyrexia in rheumatic patients, in the absence of articular and cardiac lesions, is generally due to splenopneumonia. Therefore the lungs should be carefully examined at intervals as far as the condition of the patient admits.

(4) *Tuberculous.*—Great stress is laid on the frequency of acute and subacute attacks of splenopneumonia ending

in recovery in very early or latent pulmonary tuberculosis. Where, as often happens, tuberculosis is only suspected, the appearance of splenopneumonia should always direct attention to the condition of the apices of the lungs. In some cases the attacks recur frequently and recede rapidly. The splenopneumonia in such circumstances is often pneumococcal.

*Account of Two Cases.*

I will now give a short account of two cases of my own which present the features of splenopneumonia.

Case 1.—The patient, aged 32, a labourer, was admitted with a first attack of rheumatic fever on October 28. Under the usual salicylate treatment the temperature fell on the third day after admission, but the articular pains were only slightly relieved. There was no rise of temperature for three weeks, though he never quite lost his pains. Subsequently he had several relapses of fever and articular pain. The heart was unaffected throughout. During one of these relapses on December 18, physical examination of the lungs showed slight dulness on the right side behind from the midscapular region to the base, with diminished vocal fremitus and resonance, weak breath sounds, scanty crepitations, and bronchophony over the upper border of dulness. Sputum very viscid, but clear and mucoid. A large number of organisms, including the pneumococcus, were found both microscopically and by culture. The temperature fell the same day, and in two days all physical signs had disappeared and the patient felt quite well. But four days later (the 24th) he had a rigor and the temperature rose to 105·6° F., well-marked signs of pneumonia of the left lower lobe developed (dulness and tubular breathing), and a crisis occurred on the ninth day. The patient made a good recovery. The blood was examined for micro-organisms on December 30, but the cultures remained sterile for three days.

In this case during a relapse of rheumatic fever an ephemeral pleuro-pneumonic attack, closely resembling

the splenopneumonia of Mosny and Malloizel, was succeeded after an interval of six days by a typical lobar pneumonia of the opposite lung. In the first attack the sputum was extremely viscid, but not rusty. Unfortunately, no note was made of the nature of the sputum in the second attack, though my impression is that it was distinctly rusty. It seems probable that the pneumococcus was responsible for both attacks, in which case the second would represent a relapse of the pneumococcal infection.

CASE 2.—The patient, aged 42, housewife, was admitted with symptoms resembling influenza. The illness began with vomiting, followed by severe and persistent aching pains in the limbs, but no articular swelling, pain, or tenderness. For the first five days there was a moderate degree of intermittent fever, the evening temperature varying from 102° F. to 100° F., the morning temperature 98·6° F. to 97° F. The pulse was irregular, but there was no other evidence of cardiac disease. At the base of the left lung a few crepitations were heard. There was slight cough with muco-purulent expectoration. Three days after admission, without any fresh symptoms, slight dulness to percussion was found over the lower half of the back of the right lung; over the lower third of the scapula broncho-vesicular breathing, bronchophony, and subcrepitant *râles*. At the extreme base breath sounds weak and vocal resonance diminished. Tactile vocal fremitus absent at both bases. The temperature fell to normal in two days' time. A few days later the dulness at the right base had increased slightly, and a dry rub was heard. The temperature rose again slightly for a few days, but the physical signs gradually cleared up, and the patient was discharged cured three weeks after admission.

Here was another case of pleuro-pneumonia closely conforming to the type of spleno-pneumonia described by Mosny and Malloizel. I regret that the sputum was not examined bacteriologically.

No one can doubt the existence of anomalous cases of pleuro-pneumonia like those so well described by Grancher and by Mosny and Malloizel. Cases similar to those which I have narrated might easily be multiplied. It is not an uncommon experience to meet with cases of acute febrile illness beginning with pleuritic pain or shivering, associated with pleuro-pulmonary signs, in which the temperature falls in a day or two, and the physical signs rapidly disappear. The nature of these abortive pleuro-pneumonic attacks is uncertain. Some are almost certainly pneumococcal, as shown by the presence of herpes labialis and rusty sputum. Others probably own a different cause.

The "splenopneumonic syndrome" may be a manifestation of pneumococcal pneumonia, which differs from the ordinary type only in the preponderance of pleuritic signs. To label all cases included in the definition given by Mosny and Malloizel as splenopneumonia appears to me to offer few advantages. In the first place, the designation splenopneumonia does not seem very suitable in view of the uncertainty prevailing as to the precise anatomical changes in the lung. Secondly, a classification of pneumonia on the basis of physical signs is not a practical one, in view of the great variety of signs met with in the same disease. At the same time, the careful description given by Mosny and Malloizel of the numerous cases on which their views are founded should encourage a closer study of certain ill-defined pleuro-pneumonias which will ultimately be classified from the standpoint of etiology.

## Concluding Remarks.

A review of the facts at present available justifies the statement that, with few exceptions, lobar pneumonia may be regarded as pneumococcal. Moreover, it is clear that our conception of the *rôle* of the pneumococcus in pulmonary disorders needs to be enlarged, and the pneumococcal group must include various anomalous

pleuro-pulmonary affections, among which must be placed the pulmonary congestions of French authors—"maladie de Woillez," pleuro-pulmonary congestion of Potain, and most instances of splenopneumonia.

The varying powers of resistance of the individual may be the chief factor which determines the clinical form assumed by the infection, as suggested by Rendu. At the same time, an attenuated virulence of the germ may play its part too. A combination of the two factors in varying proportions would at least provide a plausible explanation of much that would otherwise be obscure in the clinical history of the various forms of pneumonia.

I desire now, at the close of these lectures, to express my sincere thanks to Dr. Bulloch for much valuable information and advice, and also to Dr. Turnbull, Dr. Fildes, and Dr. Fearnsides for their ready help in many matters. In conclusion, Sir, allow me to convey my gratitude to you and to all those who have so patiently listened to my discourse.

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